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TUBERCULOSIS OF LUNGS IN PATIENTS WITH SARCOIDOSIS, GRANULOMA ANNULARE AND LUPUS ERYTHEMATOSUS

A COMPARISON, BASED ON ROENTGENOLOGIC STATISTICS, WITH
ITS INCIDENCE IN PATIENTS WITH PROVED TUBERCULOSIS
OF THE SKIN AND WITH DIFFERENT STAGES
OF SYPHILIS

STEPHAN EPSTEIN, M D
MARSHFIELD, WIS

The etiology of sarcoidosis (lymphogranulomatosis benigna Besnier-Boeck-Schaumann disease, sarcoid of Boeck, lupus pernio), granuloma annulare and lupus erythematosus is still undetermined. The discussion usually centers around the following possibilities: (1) a specific disease, caused by (a) *Mycobacterium tuberculosis*, (b) another specific micro-organism or (c) an unknown organism or virus, and (2) a syndrome or cutaneous reaction caused by any of a multiplicity of agents.

The association of these diseases with general tuberculosis has been used in defending as well as in refuting the possibility of a tuberculous origin. Therefore, it seems justified to report a statistical study of the incidence of tuberculosis of the lungs with these conditions.

METHOD

The statistics presented are based on the records of the radiologic department of the university dermatologic clinic at Breslau, Germany (directors, Prof. J. Jadassohn and Prof. M. Jessner), from 1925 to 1934.

The statistics concerning sarcoidosis, granuloma annulare and lupus erythematosus (table 1) are compared with analogous statistics of patients with true tuberculosis of the skin (table 2), as well as with those of syphilitic patients without tuberculous manifestations of the skin (table 3).

This seemed to afford an adequate basis for comparison. The patients came from the same environment, they were comparable as far as age and sex are concerned, and there was no selection in any group.

One disadvantage of the use of syphilitic patients as controls must be mentioned. They were examined primarily on account of the heart and aorta, it does not seem probable that active tuberculosis could escape detection, but minor residua of an old tuberculosis may have been overlooked or disregarded in some instances. If

TABLE 1—Incidence of Tuberculosis of the Lung in Patients with Sarcoidosis, Granuloma Annulare and Lupus Erythematosus

Diagnosis	Sex	Number of Patients	Average Age Years	Incidence (In Percentage) in Various Groups						Total of 1, 2 and 3
				0 Negative Findings	1 Signs of Healed Tuberculosis	2 Active Tuberculosis	2a Less Extensive Fibroid Processes	2b Extensive, Acute or Progressive Processes	3 Mottling of the Lung	
Sarcoidosis (lympho granulomatosis benigna, sarcoid of Boeck, and lupus pernio)	Total	23	41	35.8	17.0	32.1	17.0	14.2	14.2	61.2
	Male	12	42	33.4	8.3	25.0	8.3	10.7	8.3	41.6
	Female	16	41	18.8	25.0	37.5	25.0	12.5	18.1	81.2
Granuloma annulare	Total	23	25	43.5	30.5	13.0	13.0		17.0	56.5
	Male	6	25	33.3	50.0				16.7	66.7
	Female	17	25	47.0	23.5	17.7	17.7		11.8	33.0
Lupus erythematosus	Total	211	36	40.0	46.8	7.2	6.2	1.0		51.0
	Male	66	35	45.5	46.9	7.0	7.6			54.5
	Female	145	36	40.2	46.8	7.0	5.0	1.4		53.8

TABLE 2—Incidence of Tuberculosis of the Lung in Patients with True Tuberculodermas

Diagnosis	Sex	Number of Patients	Average Age Years	Incidence (In Percentage) in Various Groups					
				0 Negative Findings	1 Signs of Healed Tuberculosis	2 Active Tuberculosis	2a Less Extensive Fibroid Processes	2b Extensive, Acute or Progressive Processes	Total of 1 and 2
Tuberculosis cutis luposa (lupus vulgaris)	Total	753	31	30.3	51.7	18.0	12.4	3.6	69.7
	Male	294	29	30.0	32.0	17.4	13.3	4.1	69.4
	Female	459	33	30.0	54.7	15.3	12.0	3.3	70.0
Tuberculosis verrucosa cutis	Total	66	36	36.4	37.9	25.7	15.1	10.6	63.6
	Male	56	35	39.2	35.8	25.0	14.3	10.7	60.8
	Female	10	46	20.0	50.0	30.0	20.0	10.0	80.0
Tuberculosis cutis colliquativa (scrofuloderma)	Total	40	22	25.0	15.0	20.0	12.5	7.5	75.0
	Male	21	19	23.8	57.2	10.0	10.0		76.2
	Female	19	26	26.3	52.6	21.1	5.2	15.9	73.7
Tuberculosis cutis lichenoides (lichen scrofulosorum)	Total	8	8	25.0	50.0	25.0	25.0		75.0
	Male	3	11		66.7	33.3	33.3		100.0
	Female	5	7	40.0	40.0	20.0	20.0		60.0
Tuberculosis cutis papulonecrotica	Total (male)	4	21	50.0	50.0				50.0
Tuberculosis cutis follicularis disseminata (lupus miliaris faciei and rosacea like tuberculid)	Total	71	37	47.9	42.3	9.8	7.0	2.8	52.1
	Male	15	43	46.6	53.4				53.4
	Female	56	36	48.2	39.2	12.6	9.0	3.6	51.5
Tuberculosis cutis indurativa (erythema induratum)	Total (female)	86	26	42.0	46.5	11.5	8.1	3.4	55.0
Total of tuberculodermas	Total	1,028	31	32.7	51.2	16.1	12.0	4.1	67.3
	Male	393	29	32.1	50.1	17.8	13.2	4.6	67.9
	Female	635	32	33.1	51.9	15.0	11.2	3.8	66.9

a roentgenogram had been taken of all the syphilitic patients, the incidence of those with signs of an old tuberculosis (group 1) probably would be larger

The examinations were carried out by three examiners according to the same standards. Fluoroscopic examination was made in practically all cases, roentgenography was used as an additional method when the fluoroscopic technic indicated pathologic changes. During the last four years additional pictures were taken routinely of all patients with proved or suspected tuberculosis of the skin.

TABLE 3—Incidence of Tuberculosis of the Lung in Patients with Different Stages of Syphilis

Diagnosis		Number of Patients	Average Age, Years	Incidence (in Percentage) in Various Groups					
				0	1	2	2a	2b	Total of 1 and 2
Early syphilis (primary and secondary syphilis)	Total	280	26	69.0	27.5	2.9	2.5	0.4	30.4
	Male	132	26	65.9	30.3	3.8	3.1		34.1
	Female	148	26	73.0	25.0	2.0	2.0		27.0
Tertiary syphilis	Total	352	42	61.7	34.1	4.2	3.1	1.1	38.3
	Male	148	41	61.5	33.1	5.0	3.4	2.0	38.5
	Female	204	41	61.8	34.8	3.4	2.0	0.5	38.2
Neurosyphilis	Total	60	44	60.0	33.3	6.7	6.7		40.0
	Male	35	45	57.9	34.2	7.9	7.0		42.1
	Female	22	43	63.6	31.8	4.6	4.6		36.4
Latent syphilis (including asymptomatic neurosyphilis)	Total	1,565	37	62.3	34.0	3.7	3.0	0.7	37.9
	Male	831	40	61.9	34.5	3.6	2.8	0.8	38.1
	Female	734	34	62.7	33.4	3.9	3.3	0.6	37.3
Prenatal syphilis	Total	227	13	71.0	26.4	2.6	2.2	0.4	29.0
	Male	93	11	70.0	30.0				30.0
	Female	134	14	71.6	23.9	4.5	3.7	0.8	28.4
Total of syphilis	Total	2,484	34.5	63.7	32.6	3.7	3.1	0.6	36.3
	Male	1,242	37	62.7	33.6	3.7	3.0	0.7	37.3
	Female	1,242	32	64.7	31.6	3.7	3.2	0.5	35.3

The lungs of the patients were classified as follows

Group 0 Negative findings

Group 1 Inactive tuberculosis, as indicated or suggested by signs such as shrinking and minor fibrous shadows of the apex, calcified lymph nodes and shadows, calcified primary complex, limited motion and adhesions of the diaphragm and obliteration of the costophrenic angle

Group 2 Active tuberculosis (a) less extensive tuberculosis of the lungs, with a tendency toward fibrosis, nodular infiltrations, and enlarged mediastinal lymph nodes, or (b) extensive, acute or progressing tuberculosis, such as massive chronic fibroid tuberculosis with or without cavities, early infiltrates with cavities or miliary tuberculosis

Group 3 Mottling of the lungs (*Marmorierung*) This classification is arbitrary, it was adopted for the purpose of comparison with previous statistics. A more detailed classification may seem desirable. Roentgenologic studies performed for this special purpose¹ may use finer criteria, such as exact measurement

¹ Nolte, F. A. Röntgenologische Lungenbefunde bei extrapulmonaler Tuberkulose, *Ztschr. f. Tuberk.* 68:305-323, 1933

of the hilus and increase in this way the number of positive findings, however, my statistics are based on routine examinations

It seems to me that the adequacy of the method employed is shown by the rather striking conformity of the results in both sexes in the larger groups

COMMENT

It is the purpose of this paper to present further statistical data bearing on the relation of sarcoidosis, granuloma annulare and lupus erythematosus to pulmonary tuberculosis but not to enter deeply into the discussion of their causation

Sarcoidosis—The cause of sarcoidosis has been extensively discussed and reviewed² in recent years. As far as I can see, the majority of dermatologists still favor the tuberculous theory,³ many authors, however, consider sarcoidosis a syndrome⁴ in which tuberculosis,

2 (a) Seance spéciale du 13 mai 1934, consacrée à l'étude des sarcoïdes IV Etiologie, pathogenie, Bull Soc franç de dermat et syph 41 1296-1354, 1934 (b) Pautrier, L M Les tuberculides, in Darier, J, and others Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol 3, pp 675-732 (c) Volk, R Tuberkulose der Haut, in Jadassohn, J Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol 10, pt 1, pp 386-404 (d) Fellner, M Die Hauttuberkulose, Dermatologica 80 108-123, 1939

3 (a) Andrews, G C Sarcoidosis, in Diseases of the Skin, ed 2, Philadelphia, W B Saunders Company, 1938 (b) Belote, G H Lupus Erythematosus Disseminatus Its Present Status, Arch Dermat & Syph 39 793-806 (May) 1939 (c) Goeckermann, W H Sarcoids and Related Lesions Report of Seventeen Cases, Review of the Recent Literature, ibid 18 237-262 (Aug) 1928 (d) Jadassohn, J Dermatologie, Vienna, Weidmann & Co, 1938 (e) Montgomery, H Histopathology of Various Types of Cutaneous Tuberculosis, Arch Dermat & Syph 35 698-715 (April) 1937 (f) Nomland, R Hematogenous Cutaneous Tuberculosis (Sarcoid) in Negroes Report of Six Cases, ibid 30 59-75 (July) 1934 (g) Sulzberger, M B Sarcoid of Boeck (Benign Miliary Lupoid) and Tuberculin Anergy, Am Rev Tuberc 28 734-745, 1933 (h) Wise, F, and Sulzberger, M B Editorial Comment, in Yearbook of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc, 1937, p 151 (i) Ramel, E, abstracted, Wise, F, and Sulzberger, M B Yearbook of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc, 1936, p 362 (j) Schaumann, J, and Bostrom, G On the Cellular Sensitivity to Tuberculin in Lymphogranulomatosis Benigna Schaumann as Exhibited in Examinations of Isolated Slices of Skin, Acta dermat-venereol 18.90-101, 1937 (k) Grillo, V Contributo alla malattia di Besnier-Boeck, una fase sarcoidea della infezione tubercolare, Gior ital di dermat e sif 79 647-669, 1938, Riproduzione delle lesioni istologiche della malattia di Besnier-Boeck-Schaumann in gangli linfatici di cavie inoculate in peritoneo con spappolato di tessuto (sarcoideo), Arch ital di med sper 4 515-522, 1939 (l) Cortella, E Sopra un caso di malattia di Schaumann-Besnier-Boeck e di sarcoide Darier-Roussy, Riforma med 54 1339-1346, 1938

4 Michelson, H E, and Becker, F T Uveoparotitis A Sarcoid Reaction, Arch Dermat & Syph 39 329-344 (Feb) 1939 Danbolt, N, and Brandt, A Sarcoidähnliche Hauttuberkulose, durch Huhnertuberkelbazillen hervorgerufen, Arch f Dermat u Syph 178 76-86, 1938

syphilis and other diseases, such as leprosy⁵ and leishmaniasis,⁶ play roles or classify it as a separate disease of unknown origin⁷

My statistics (table 1) show a relatively high incidence of active pulmonary tuberculosis. Of 28 patients, 4 suffered from progressive tuberculosis and 5 from a less extensive fibroid form; more or less evidence of mottling of the lungs was found in 4 more. The total number of observations, however, is small.

More impressive are those cases in which active tuberculosis of the lungs developed during observation, with or without change of the clinical picture.⁸ Two of my patients belong to this group. A woman suffering from lupus pernio was free from pulmonary involvement except for shadows in one apex in 1919. In 1927 the roentgenogram showed definite mottling. A fulminating type of tuberculosis developed in 1928, from which she died. The other patient, a man, suffered for years from circinate sarcoid-like lesions of the cheek, without signs of an active tuberculosis of the lungs. Years later active tuberculosis developed, from which he died. Before his death the sarcoid lesions changed to lesions of lupus vulgaris.

It may be of interest to report the sensitivity to tuberculin (positive anergy of Jadassohn) and the incidence of osteitis tuberculosa multiplex cystoides (Jungling), as given in tables 4 and 5. Two results may be stressed, with the necessary caution on account of the small number of cases: (1) One half of the patients, a rather high figure when compared with other statistics,⁹ reacted to old tuberculin in a dilution of 1:5,000, and (2) nearly all (6 of 7) patients with osteitis multiplex cystoides gave negative reactions. The tuberculous theory, at least for the group reported on, is supported by the statistics presented.

5 Jordon, J. W., and Osborne, E. D. Besnier-Boeck's Disease. Report of Two Cases of Extensive Involvement, *Arch. Dermat. & Syph.* **35**:663-684 (April) 1937. Pillsbury, D. M. Pulmonary Tuberculosis. Sarcoid, *ibid.* **33**:763-764 (April) 1936.

6 With, T. K. Benign Lymphogranulomatosis with Special Consideration of Its Relation to Tuberculosis and Uveoparotid Fever, *Nord. med. tidskr.* **12**:1787-1795, 1936, abstracted, *Zentralbl. f. Haut- u. Geschlechtskr.* **57**:524, 1938.

7 Kissmeyer, A., and Nielsen, J. Notes sur l'étiologie des sarcoïdes de Boeck, *Acta dermat.-venereol.* **14**:283-286, 1933. Pautrier, L. M. Les lésions oculaires de la maladie de Besnier-Boeck-Schaumann (Le syndrome de Heerfordt), *Arch. d'opht.* **2**:689-696, 1938.

8 (a) Bonnevie, P., and With, T. K. Ein Fall von Sarkoid Boeck (Lymphogranulomatosis benigna) zur Heilung gekommen unter Entwicklung einer aktiven multiplen Tuberkulose und unter Änderung der Tuberkulinreaktivität, *Arch. f. Dermat. u. Syph.* **175**:407-411, 1937. (b) Goldschmidt, W. N. Ueber circinarrverrucose Umwandlung bei einem Sarkoid Boeck und eine ähnliche Form bei Lupus vulgaris, *ibid.* **149**:331-338, 1925. (c) Funk, C. F. Boecksches Sarkoid, Lupus pernio und Lungenbeteiligung, *ibid.* **167**:560-577, 1933. (d) Nolte¹, Volk^{2c}.

9 Schaumann and Bostrom^{3j}, Funk^{8c}.

Granuloma Annulare—As far as the cause of granuloma annulare is concerned, no definite trend in the general opinion is noticeable¹⁰ The combination with other manifestations of tuberculosis of the skin,¹¹ the relation to the sarcoid group¹² and to tuberculosis papulonecrotica,¹³ the histologic observations, the positive anergy and the occurrence of mottling of the lungs are arguments for those who assume its tuber-

TABLE 4—*Tuberculin-Sensitivity in Patients with Sarcoidosis and Granuloma Annulare **

Diagnosis	Sex	Number of Patients	Average Age, Years	Old Tuberculin, Dilution of 1:3,000			
				Positive Results		Negative Results	
				Number	Per Cent	Number	Per Cent
Sarcoidosis (lymphogranulomatosis benigna, sarcoid Boeck and lupus pernio)	Total	22	42	11	50.0	11	50.0
	Male	9	43	4	44.4	5	55.6
	Female	13	42	7	53.6	6	46.2
Granuloma annulare	Total	14	24	6	42.9	8	57.1
	Male	4	21	1	25.0	3	75.0
	Female	10	25	5	50.0	5	50.0

* These cases are identical with those in table 1, but records of only 22, 14 and 10 cases respectively, were available

TABLE 5—*Occurrence of Osteitis Cystica Multiplex in Patients with Sarcoidosis **

Sex	Number of Patients	Average Age, Years	Osteitis Cystica Occurred in		Total
			Tuberculin Positive Patients	Tuberculin Negative Patients	
Total	19	40	1	6	7
Male	7	42		3	3
Female	12	38	1	3	4

* These cases are identical with those in table 1, but records of only 22, 14 and 10 cases respectively, were available

culous origin. But this theory is far from being generally accepted. My statistics are not conclusive. They may be compared with the figures

10 (a) Jacobi, F. Granuloma annulare, in Jadassohn, J. Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 10, pt. 1, pp. 796-822. (b) Michael, J. C. Etiology of Granuloma Annulare, with Special Reference to the Tuberculous Theory, Arch. Dermat. & Syph. 29: 189-205 (Feb.) 1934. (c) Goodman, M. H., and Ketron, L. W. Granuloma Annulare. Report of Unusual Cases with Comments on the Histology of the Disease, ibid. 33: 473-494 (March) 1936. (d) Fellner.²⁴

11 Halliwell, E. O., and Ingram, J. T. Granuloma Annulare, Brit. J. Dermat. 47: 319-340, 1935.

12 Martenstein, H., and Noll, R. Statistische Untersuchungen über die Tuberkulinreaktion, Arch. f. Dermat. u. Syph. 158: 409-420, 1929.

13 Pinkus, H. Ueber atypische Tuberkulide, zugleich ein Beitrag zur Ätiologie des Granuloma annulare, Arch. f. Dermat. u. Syph. 170: 194-222, 1934.

compiled by Michael^{10b} from 50 cases in the literature, he found no tuberculosis in 70 per cent, healed tuberculous lesions in 4 per cent, questionable changes in 10 per cent and active tuberculosis in 16 per cent

Table 4 shows the high incidence of negative reactions to tuberculin, which is in agreement with other statistics¹⁴ The age may partly account for these results, the average age of those with negative reactions being 18 (5 to 36), as compared with 32 (18 to 49) in the group with positive reactions

Lupus Erythematosus—The discussion of the cause of lupus erythematosus is still a favorite topic of dermatologic meetings¹⁵ The tuberculous origin (Besnier) of this disease, as assumed by the French and part of the Austrian, German and Swiss schools, has never appealed greatly to the American and British dermatologists¹⁶ Numerous studies have been devoted in recent years to the relation between lupus erythematosus and tuberculosis,¹⁷ the tuberculous theory still has its supporters¹⁸

14 Martenstein and Noll¹² Michael^{10b}

15 (a) Belote, G H, and Ratner, H S V The So-Called Libman-Sacks Syndrome Its Relation to Dermatology, Arch Dermat & Syph 33:642-664 (April) 1936 (b) Engman, M F, Jr Early Acute Lupus Erythematosus, ibid 35:685-697 (April) 1937 (c) Mook, W H, Weiss, R S, and Bromberg, L K Lupus Erythematosus Disseminatus, ibid 24:786-829 (Nov) 1931 (d) Séance speciale du 14 mai 1939, consacré au lupus érythémateux Etiologie Pathogénie, Bull Soc. franç de dermat et syph 46:1030-1177, 1939

16 (a) Macleod, J M H Lupus Erythematosus Some Observations on Its Etiology, Arch Dermat & Syph 9:1-12 (Jan) 1924 (b) Montgomery, H Disseminate Lupus Erythematosus as a Systemic Disease, in Christian, H A Oxford Medicine, New York, Oxford University Press, 1939, vol 4

17 (a) Cannon, A B, and Ornstein, G G The Tubercle Bacillus as an Etiologic Factor in Lupus Erythematosus, Arch Dermat & Syph 12:691 (Nov) 1925 (b) Ehrmann, S, and Falkenstein, F Ueber Lupus erythematoses, Arch f Dermat u Syph 141:408-506, 1922 (c) Keil, H Relationship Between Lupus Erythematosus and Tuberculosis A Critical Review Based on Observation at Necropsy, Arch Dermat & Syph 28:765-779 (Dec) 1933 (d) Pautrier, L M Lupus érythémateux, in Darier, J, and others Pratique nouvelle dermatologique, Paris, Masson & Cie, 1936, vol 3, pp 733-824 (e) Ramel, E Neuere Beobachtungen und Anschauungen über die Beziehungen des Lupus erythematoses zur Tuberkulose, Med Klin (Extrapulmonale Tuberkulose supp 3), 1925, pp 11-24 (f) Throne, B Lupus Erythematosus A Clinical Study, Arch Dermat & Syph 12:33-40 (July) 1925 (g) Symposium Was spricht für und gegen die tuberkulose Natur des Lupus erythematoses? Dermat Wchnschr 99:1346-1356, 1934 (h) Veiel, F Lupus erythematoses, in Jadassohn, J Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol 10, pt 1, pp 687-795 (i) Weidman, D, and Gilman, R L A Case of Acute Disseminated Lupus Erythematosus Necropsy Disclosing Acute Endocarditis but Not Tuberculosis, Brit J Dermat 43:641-647, 1931 (j) Macleod^{16a}

18 Stokes, J H, in discussion on Engman^{15b} Cannon and Ornstein^{17a} Ehrmann and Falkenstein^{17b} Marchionini^{15d} Ramel^{15d}

but is losing ground¹⁰ At present the majority apparently consider lupus erythematosus either to be a syndrome (Jadassohn) caused by various agents, such as infections, drugs²⁰ or mineral poisons²¹—in other words, a “reaction cutanée” (Brocq) “based on a certain form of immunologic response”²⁰—or a clinical entity of its own, caused either by a known agent, such as the streptococcus²² or a focal infection,²³ or by an unknown organism²⁴

The association of pulmonary tuberculosis and lupus erythematosus has been a subject of wide controversy The literature lists positive findings from 5 per cent¹⁰ to 100 per cent²⁵ Differences of methods, small numbers of cases, lack of comparison with adequate controls and other factors, such as different incidence of tuberculosis in various countries and errors in diagnosis, may account partly for these discrepancies They render the comparison and evaluation of these statistics difficult if not impossible

My statistics of 211 cases constitute—so far as I can see—the largest single report on this subject The results are based exclusively on roentgenologic examinations of the lungs, other forms of tuberculosis, such as involvement of the lymph nodes, have not been considered The incidence of active tuberculosis (7.2 per cent) is decidedly lower than average in persons with true tuberculosis of the skin or in any single group of patients with this condition large enough for comparison (table 2) On the other hand, the percentage is higher than average among syphilitic patients but is not far above the figure found in patients with neurosyphilis (6.7 per cent) If one considers the figures of inactive tuberculosis, those of lupus erythematosus (46.8 per cent) rank closer to those of cutaneous tuberculosis (51.2 per cent) than to those of syphilis (32.6 per cent), however, the comparison with the syphilitic

19 Cummer, C. L. Etiology of Lupus Erythematosus Occurrence in the Negro, *Arch Dermat & Syph* **33**:434-445 (March) 1936 Belote^{3b} Keil^{17c}

20 Sulzberger, M. B., in discussion on Engman^{15b} Rost^{15d}

21 Ludy, J. B., and Carson, E. F. Lupus Erythematosus Increased Incidence, Hematoporphyrinuria and Spectroscopic Findings, *Arch Dermat & Syph* **35**:403-416 (March) 1937

22 Barber, H. W. A Case of Lupus Erythematosus Associated with Streptococcal Infection of the Tonsils, *Brit J Dermat* **31**:186-193, 1919, cited by Ramel^{17e} O'Leary, P. A., in discussion on Engman,^{15b} and on Mook^{15e}

23 Tolman, M. M., in discussion on Ludy and Carson²¹ Ayres, S., Jr., in discussion on Mook^{15e} Throne^{17f}

24 Lindenberg, A. Contribuição ao estudo da etiologia do lupus erythematosus, *Arch de dermat et syph de São Paulo* **1**:147-149, 1937, abstracted, *Zentralbl f Haut- u Geschlechtskr* **59**:307, 1938 Belote^{3b}

25 Kren, O. Zur Klarung der Pathogenese des Lupus erythematosus acutus, *Wien med Wchnschr* **86**:680-683, 1936, abstracted, Wise, F., and Sulzberger, M. B. Yearbook of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1937, pp 224-225 Ehrmann and Falkenstein^{17b}

controls is somewhat hampered in group 1 by the previously mentioned fact that they were primarily examined on account of the heart and aorta

My results agree with those of others²⁶ I do not think that these statistics can be used to support the tuberculous theory

INCIDENCE OF TUBERCULOSIS OF THE LUNGS IN PATIENTS WITH TRUE TUBERCULOSIS OF THE SKIN

Three facts seem noteworthy

1 The occurrence of active tuberculosis of the lungs in patients with different types of cutaneous tuberculosis shows great variations, being highest in patients with tuberculosis verrucosa and lowest in patients with the lupus miliaris-rosacea-like tuberculid group of conditions

2 The incidence of progressive pulmonary tuberculosis in patients with lupus vulgaris as found in my series agrees well with other statistics²⁷ The fact that 16 per cent of these patients exhibited signs of active tuberculosis of the lungs seems to contradict the general belief²⁸ that the combination of lupus vulgaris and active tuberculosis is unusual Apparently, there are two different problems: lupus vulgaris as a complication of tuberculosis of the lungs is exceedingly rare, the opposite, however, pulmonary tuberculosis as a complication of lupus vulgaris, is not so unusual Of course, this becomes more evident when a larger series such as mine is studied over a period of many years

3 Men and women with lupus vulgaris show the same incidence of all types of pulmonary conditions This is in contradistinction to some previous statistics²⁷ based on a smaller amount of material

INCIDENCE OF TUBERCULOSIS OF THE LUNGS IN PATIENTS WITH DIFFERENT STAGES OF SYPHILIS

The incidence of tuberculosis of the lungs is slightly higher in patients with late stages of syphilis than in those with early stages It remains

26 Goeckerman, W H Is Lupus Erythematosus Discoides Chronicus Due to Tuberculosis? Arch Dermat & Syph **3**:788-801 (June) 1921 Pautrier and Schaaff^{15d}

27 (a) Martenstein, H Die Lungentuberkulose als Komplikation der Tuberkuloderme, Arch f Dermat u Syph **131**:168-179, 1921, (b) Weitere Mitteilung über die Lungentuberkulose bei Tuberkulodermen, *ibid* **140**:341-345, 1922 (c) Memmesheimer, A M Untersuchungen über den Einfluss des Hauttuberkulose auf die Lungentuberkulose, *ibid* **174**:511-517, 1936 (d) Schmitt, K Hauttuberkulose und Lungentuberkulose, Strahlentherapie **63**:52-56, 1938

28 Fox, H Lupus Vulgaris and Pulmonary Tuberculosis, Arch Dermat & Syph **40**:154-155 (July) 1939 Cannon, B A, Combes, F C, and MacKee, G M, in discussion on Fox

an open question whether this fact—if not altogether incidental—is due to differences of age or whether it reflects an influence of the existing syphilis

SUMMARY

Statistics concerning the incidence of tuberculosis of the lungs in 28 patients with sarcoidosis (lymphogranulomatosis benigna, Besnier-Boeck-Schaumann disease, sarcoid of Boeck, lupus pernio), in 23 patients with granuloma annulare and in 211 patients with lupus erythematosus are presented and compared with analogous statistics of 1,028 cases of ascertained tuberculosis of the skin and 2,484 cases of syphilis

Sensitivity to tuberculin in patients with sarcoidosis and granuloma annulare and occurrence of osteitis tuberculosa multiplex cystoides (Jungling) in sarcoidosis are reported

EARLY SYPHILITIC LESIONS MISTAKEN FOR DERMATOPHYTOSIS

EVAN W THOMAS, M D

AND

SAMUEL M BLUEFARB, M D

NEW YORK

Among the commonest lesions of secondary syphilis are moist papules, which are usually found about the genitals and anus. When fused in plaques they form the familiar condylomata lata of secondary syphilis, and it has long been known that their growth is favored by the moisture, heat and friction of opposing surfaces.

One of the less common places for such lesions, and one that may be overlooked and thus cause an error in diagnosis, is between the toes, especially if the patient has an associated dermatophytosis¹. In our experience it is not uncommon to see patients who have attended clinics and have been treated for dermatophytosis when there was an associated syphilitic process present. The moist, boggy skin with macerated opposing surfaces that characterizes fungous infections between the toes offers an ideal place for the localization of *Spirochaeta pallida* and the formation of moist papules, which in some cases present the typical picture of condylomata lata. Ch'in¹ reported 3 such cases in Shanghai in 1932, but, so far as we know, similar reports from this country have been extremely rare.

At Bellevue Hospital secondary syphilitic lesions between the toes have been noted a number of times. Between September 1938 and February 1940, 6 cases were observed, and in 5 of these treatment had been given for varying lengths of time for stubborn dermatophytosis. When the lesions failed to respond to the usual treatments with potassium permanganate and compound ointment of benzoic acid U S P, the patients were referred to the dermatologic wards, where the presence of early syphilis was diagnosed and confirmed in every case by the finding of *S. pallida* on dark field examination. In each patient spirochetes were found in serum taken from lesions between the toes. Dark

From the Department of Dermatology and Syphilology, New York University College of Medicine, and the Department of Dermatology and Syphilology, Third Medical (New York University) Division, Bellevue Hospital, service of Dr. Edward R. Maloney.

1 Ch'in, T. L. Syphilis of Toes Resembling Fungus Infection (Hongkong Foot). Report of Three Cases, Chinese M J 46:60-63 (Jan) 1932.

field examination of fluids taken from the lesions of dermatophytosis in patients without early syphilis have never shown similar spirochetes in our experience. In addition, all of the patients in whom *S. pallida* was found had strongly positive Wassermann reactions of the blood.

In 4 of the 6 cases the diagnosis of early syphilis could have been made from other clinical manifestations of the disease besides the lesions between the toes. Failure to strip the patients or to elicit an adequate history was solely responsible for the delay in diagnosis. One gave a history of sores about the anus of three months' duration and foul-smelling sores between the toes for about the same period. At the time of examination he had, in addition to the lesions about the anus and between the toes, flat papules on the shaft of the penis and a sore throat. Two patients had primary lesions on the penis as well as scrotal lesions and scattered papules on the trunk and extremities, including the palms and soles in 1 case. All had dermatophytosis, and all but 1 had been treated for this condition after the appearance of early syphilitic lesions. In 3 cases the condition was less easily diagnosed, and these merit more detailed report.

REPORT OF CASES

CASE 1—Probable chancre between the toes

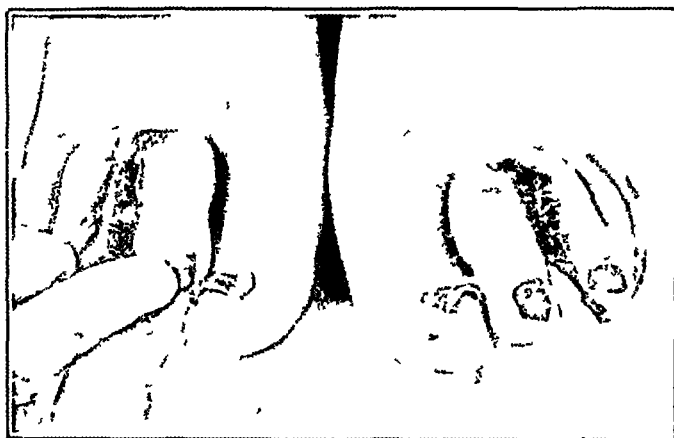
A Negro aged 20 was admitted to the wards of Bellevue Hospital on Sept. 12, 1938. He gave a history of "ringworm" between the toes of both feet of over one year's duration. Examination revealed the characteristic lesions of dermatophytosis on both feet, but in addition between the fourth and fifth toes of his right foot he had a single, deep ulceration. The ulcer was well demarcated, indurated and covered by a rather firm necrotic callus. The surrounding skin showed considerable maceration. He had bilateral discrete, nontender inguinal nodes and a single large, visible node in the right femoral region. This was considered a satellite bubo, in view of the other findings. There were no other cutaneous lesions, but the patient had a red throat and hypertrophied tonsils. The Wassermann reaction of the blood was strongly positive, and dark field examination of the ulcer between the toes revealed spirochetes typical of *S. pallida*. From the history obtained this ulcer had started about ten weeks prior to admission and had been treated locally as dermatophytosis.

Within two weeks after the starting of antisyphilitic treatment with arsphenamine the ulcer was entirely healed, though the dermatophytosis remained. The femoral node had become reduced in size during the same period. The diagnosis of chancre seemed justified in this case, though nothing could be elicited from the patient's history as to how he contracted a primary syphilitic lesion in so unusual a place.

CASE 2—Prolonged duration of moist papules between the toes

A white man aged 34 was admitted to one of the surgical wards of Bellevue Hospital on Nov. 16, 1939, because of ulcerations between the toes, which had become so painful that he had been unable to walk for the previous six weeks. During this time he stated that he had lost 10 pounds (4.5 Kg.) in weight. He was transferred to the dermatologic wards of the hospital, with a diagnosis of dermatophytosis and probable syphilis. Apart from the history of the condition

of his feet the patient volunteered no information, and such data as could be obtained may not have been entirely accurate. Repeated questioning, however, elicited consistent answers regarding previous genital lesions. He maintained that he had first noticed an ulcer on the penis some time in February 1939. He was not sure how long this lasted, but apparently its duration was at least two months. Some time in March, about two months prior to the appearance of papules on the genitalia, he first noted sores between his toes. As nearly as he could recall, in May a sore throat developed and he noted red papules on the shaft of his penis and scrotum. He was again vague about the duration of these lesions but was sure they had not been present for at least two months prior to admission. He stated that he had been treated intermittently for "athlete's foot" for six or seven months prior to admission to Bellevue Hospital and that he had been annoyed by the foul odor of his feet during that time. The sores, however, had become decidedly painful only about two months prior to admission, after the use of a "potash solution" locally. The odor had become even more offensive during this period.



Secondary syphilitic lesions mistaken for dermatophytosis

On examination the scar of the penile lesion which had started nine months prior to admission was still plainly visible. No other lesions could be found about the genitals or anus. He had no cutaneous manifestations apart from those between the toes. The photograph was taken after much of the superficial debris had been removed and most of the edema had subsided. Beneath the crusts typical small condylomata lata were visible between all of the toes. Numerous spirochetes were seen on dark field examination of the fluid oozing from the lesions. They had the typical appearance of *S. pallida*, and the Wassermann reaction of the patient's blood was strongly positive. In addition he had a red throat with small papules on the anterior pillars, that disappeared entirely after one injection of mapharsen. He stated that he did not have a sore throat at the time of admission but that his throat had been sore for some months prior to admission. Within a week after the first injection of mapharsen there was great improvement of the lesions between the toes, and within two weeks they were entirely healed except for the evidences of persisting fungous infection. The throat cleared within four days after treatment was started.

If the patient's history can be believed, this case is an unusual one of secondary syphilitic lesions persisting for months between the toes and probably in the throat long after other secondary manifestations had disappeared. We have observed cases of early syphilis in which sore throats remained for weeks after the cutaneous

lesions had disappeared, but in this patient moist papules continued between the toes for at least two months after they had entirely disappeared from the genitals. The trauma of walking, local treatments and the associated dermatophytosis between the toes evidently favor the prolonged continuation of moist papules with active spirochetes after the skin elsewhere has become resistant to the presence of spirochetes.

CASE 3—Relapsing secondary syphilis with moist papules between the toes

A white man aged 26 was admitted to the dermatologic wards of Bellevue Hospital on Feb 27, 1940, because of foul-smelling sores between the toes of both feet and large fleshy papules on his scrotum. He gave a history of having had a chancre on the penis in December 1935, at which time he attended a department of health clinic. A report of the findings at that time, obtained from the clinic, included the facts that *S. pallida* was found in the chancre and that the Wassermann reaction of his blood was strongly positive. Between December 1935 and June 1936 he received fourteen injections of mapharsen and three injections of a bismuth compound, irregularly spaced. He had no treatment after that. About Jan 25, 1940, he noticed papules on his scrotum and sores between his toes. He had had "athlete's foot" for several months prior to this date and went to a clinic because of his feet. A routine Wassermann test of the blood gave a positive result, and his scrotal lesions were then discovered. *S. pallida* was found on dark field examination of the sores between the toes. The unusual feature of this case was the four year interval between his initial lesion and the relapsing secondary manifestations.

SUMMARY AND CONCLUSIONS

Dermatophytosis between the toes provides a favorable soil for the localization and growth of *S. pallida*, with the formation of infectious early syphilitic lesions.

Six cases of such a condition are reported, in 1 of which the lesion was probably a chancre.

Moist papules between the toes, like lesions in the throat, may persist after all other cutaneous lesions have disappeared.

TURBAN TUMORS

REPORT OF A CASE WITH UNUSUAL PATHOLOGIC FINDINGS,
INCLUDING BOTH EPIDERMAL AND DERMAL NEVI

WILBERT SACHS, M D

JERSEY CITY, N J

AND

PERRY M SACHS, M D

NEW YORK

Congenital and acquired multiple tumors of the scalp are infrequently reported in the literature. They have been described by different authors under many titles, such as turban tumor, naevo-epithelioma nodosum, cylindroma, multiple benign epithelioma, fibroma multiplex, fibroma capitis, endothelioma capitis and sweat gland carcinoma. The diversity of names resulted from the variation of histologic observations and interpretations made by past investigators.

In 1841 Ancell¹ described a case of tumors of the scalp. Baker, Kaposi and Orro,² as well as Poncet³ and Cohn,⁴ considered the condition some form of sarcoma. Spiegler⁵ concluded that the growths in the cases of Ancell, Kaposi, Poncet and Cohn were endotheliomas, or sarcomas. An example of endothelioma of the scalp had been presented by Mulert⁶ two years previously. The differentiating feature observed in the descriptions of Baker, Kaposi and Orro was a history of trauma preceding the development of the tumors.

About the same time Barrett⁷ published a report of a mother and daughters all with similar lesions, to which he attached the name

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University

1 Ancell, H. History of a Remarkable Case of Tumours, Developed on the Head and Face, Accompanied with a Similar Disease in the Abdomen, *M. Chir. Tr.* 227, 1842, reviewed, *Arch. Surg.* 6:119, 1895.

2 Cited by Crocker, H. R. Diseases of the Skin, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1903, p. 1027.

3 Poncet, A. Note sur une variété de tumeurs confluentes du cuir chevelu, *de chir.*, Paris 10:244, 1890.

4 Cohn, I. E. Multiple Sarcoma of the Scalp, *J. Cutan. Dis.* 10:398, 1892.

5 Spiegler, E. Ueber Endotheliome der Haut, *Arch. f. Dermat. u. Syph.* 163, 1899.

6 Mulert, D. Ein Fall von Multiplen Endotheliomen der Kopfhaut, *Arch. f. Chir.* 54:658, 1897.

7 Barrett, J. W., and Webster, P. Multiple Sudoriparous Adenomata Occurring on the Scalp and Face in Three Members of the Same Family, *Brit. M. J.* 72, 1892.

multiple sudoriparous adenomas. Later Fick⁸ denouced the term endothelioma, and Frieboes⁹ concluded that most of these conditions were examples of epithelial tumors of slow growth. Cylindroma, a substitute term for endothelioma, originated with Billroth,¹⁰ and many examples of this are to be found in the literature. Jones, Alden and Bishop¹¹ described their case as one of sweat gland carcinoma of low grade malignancy.

Stillians,¹² in his series of cases, concluded that cylindromas are basal cell epitheliomas which may originate from the surface epithelium or the hair follicle. He preferred the name naevo-epithelioma adenoides, suggested by Hoffman.¹³ Zakon¹⁴ also reported a case under this heading. Binkley,¹⁵ in describing his series, slightly altered this name, to naevus epitheliomato-cylindromatosus.

Jones, Alden and Bishop, Stillians and Binkley, in their respective articles, have thoroughly reviewed the literature to the present, including the earliest cases, occurring in the middle of the last century. In contrast, our case of turban tumor does not present the same features as those heretofore described.

REPORT OF CASE

History—L. W., a Negro aged 19, was admitted to the Medical Center of Jersey City in March 1931, with pneumonia. An uneventful recovery followed. Coincidentally, he presented multiple tumors on the right side of his scalp. The patient stated that all the growths had been present since birth, and none had spontaneously appeared or disappeared thereafter. They enlarged in proportion with the growth of his head. There were never any subjective symptoms or any bleeding, oozing, ulcerations or infections. Several physicians at various times advised against therapeutic intervention.

The family history was irrelevant and no member had any similar condition.

Physical Examination—Covering the right parietal and occipital regions of the scalp and extending medially to about 1 inch (2.5 cm.) of the midline and laterally to about 1 inch above the lobe of the ear were numerous tumor masses

8 Fick, J. The Impracticability of "Endothelioma" as a Working Hypothesis, *J. Cutan. Dis.* 50:444, 1912.

9 Frieboes, W. Beitrag zur Klinik und Histopathologie der gutartigen Hautepitheliome, Berlin, S. Karger, 1912.

10 Cited by Dalous, E. Le cylindrome de la peau, *Arch. de med. exper. et d'anat. path.* 15:796, 1903.

11 Jones, J. W., Alden, H. S., and Bishop, E. L. Turban Tumor, or Sweat Gland Carcinoma, *Arch. Dermat. & Syph.* 26:656 (Oct.) 1932.

12 Stillians, A. W. Nevo-Epithelioma Adenoides (Cylindroma) of the Scalp, *Arch. Dermat. & Syph.* 26:481 (March) 1933.

13 Hoffman, E., cited by Gans, O. Histologie der Hautkrankheiten, Berlin, Julius Springer, 1928, vol. 2, p. 297.

14 Zakon, S. J. Naevo-Epithelioma Adenoides (Cylindroma) of the Scalp, *Arch. Dermat. & Syph.* 40:945 (Dec.) 1939.

15 Binkley, G. W. Naevus Epitheliomato-Cylindromatosus, *Arch. Dermat. & Syph.* 37:289 (Feb.) 1938.

proximately a hundred) These varied from 3 mm to 3 cm in diameter, the range being about 1 cm Over the parietal area the lesions were comparatively ill, the largest being about 1.5 cm These were closely massed, most of them were pedunculated, and some were fused together The tumors could be separated easily, thereby revealing their point of attachment to the scalp They appeared unlike the cerebral convolutions Over the anterior occipital region the growths were more uniform in size, varying from 0.25 to 0.75 cm in diameter, they were fewer, and they arose directly from the scalp The largest lesion, located in the posterior occipital region, was attached to the scalp by a pedicle 0.5 cm in diameter The mass overhung the upper part of the neck Two smaller masses arose from the upper and lower poles of this larger one, the former 1 cm and the latter 1.5 cm in diameter



Fig 1—Turban tumor in a Negro aged 19

The tumors were mostly spherical, although some were pear shaped (like the largest one) and others were flat. They ranged from light brown to almost black, the surface being lighter than parts nearer the scalp The surface was tense, firm and smooth except in a few pitted zones The lesions themselves were entirely devoid of hair, however, the hair between the lesions is like that on the rest of the scalp

The individual tumors were not movable on the deeper parts, but the entire area containing the tumors and the underlying scalp were easily raised off the skull This area of the scalp appeared to be more loosely attached to the skull than the rest

Otherwise, physical examination of the patient revealed no abnormalities A roentgenogram of the skull was normal The Wassermann reaction of the blood was negative

Histologic Examination—The section was large and round and was covered by epidermis except at its base. In part the epidermis was thin and flattened, and in part it was thickened, and in the latter areas the cells were arranged in bands and strands, some of which anastomosed to form a coarse network (fig 2). For the greater part, the basal cell margin was uniform, orderly and intact. However in some areas there were small nests of epithelial cells in the basal cell margin (fig 2). Where epidermis was thin and flattened there were no rete pegs and papillary bodies.



Fig 2—An intraepidermal nevus and a junction type nevus (high power)

Throughout the midcutis there was in bandlike fashion a mass of cells (considered by many to be of epithelial origin), some arranged in groups and some isolated (fig 3). The entire upper part of the cutis was free of these cells. With high power these cells were seen to have large round hyperchromatic nuclei and definite lightly stained cell bodies. In places the cell outlines were easily distinguished. Many of the cells were multinucleated. There was a small amount of pigment present in and about these cells. The nuclei of all the cells were fairly uniform in size and shape. The nests of cells in the lower border of the epidermis were composed of cells of a similar nature.

The entire connective tissue framework was moderately increased, in some areas taking on a whorl formation (fig 4) In some regions there were numerous dilated thin-walled blood vessels, some of which were filled with blood elements



Fig 3—An intradermal cellular nevus (low power)

(fig 5) Nowhere in the section was there any inflammatory process Hair follicles or sebaceous glands were not present Throughout the entire cutis framework there was sparse diffuse infiltrate composed of spindle cells and fibroblasts

The entire tissue was an example of a congenital malformation consisting of a hyperplastic intraepidermal cellular nevus, a junction type nevus, an intradermal cellular nevus (origin of the two latter is still a matter of dispute) and also the mesenchymal process, such as the fibromatous nevus within which was an angioma. The entire picture fit in with a mixed nevus.

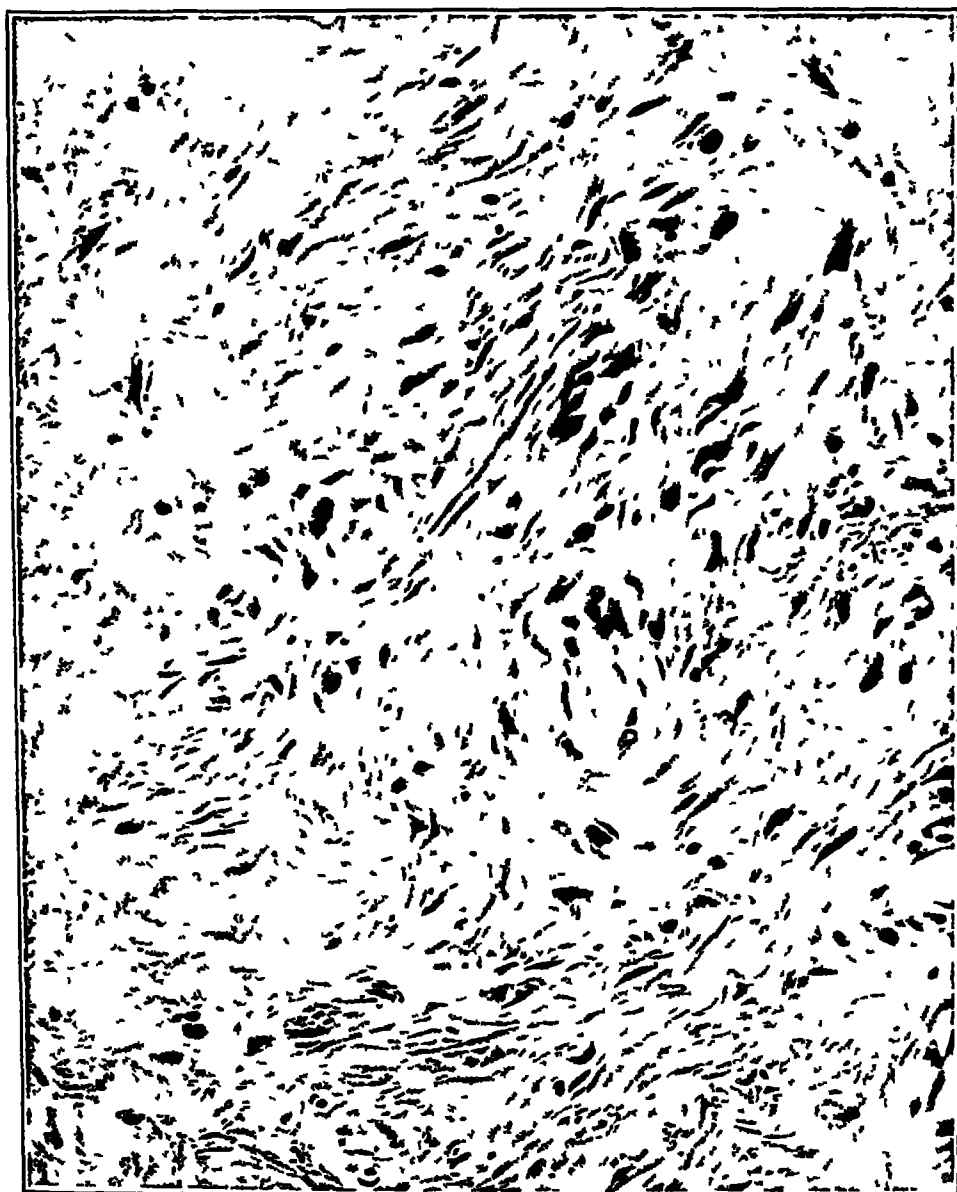


Fig 4—A fibromatous nevus (high power)

COMMENT

Obviously, turban tumor is not a histologic entity but a clinical term. Microscopic study is necessary for the more accurate diagnosis. Our case shows the clinical features seen in turban tumors, however, the histologic features are not in accord with those previously reported.

The only case similar to ours was mentioned by Binkley. Clinically the tumor in his case was called a cylindroma, it grew rapidly and metastasized after injury. At postmortem examination the diagnosis of nevocarcinoma was made. Binkley inferred from this that any tumors of the scalp accompanied by rapid growth and metastasis should not be called turban tumor. Furthermore, this author claimed that malignant tumors of the scalp, unless originating from the benign basal

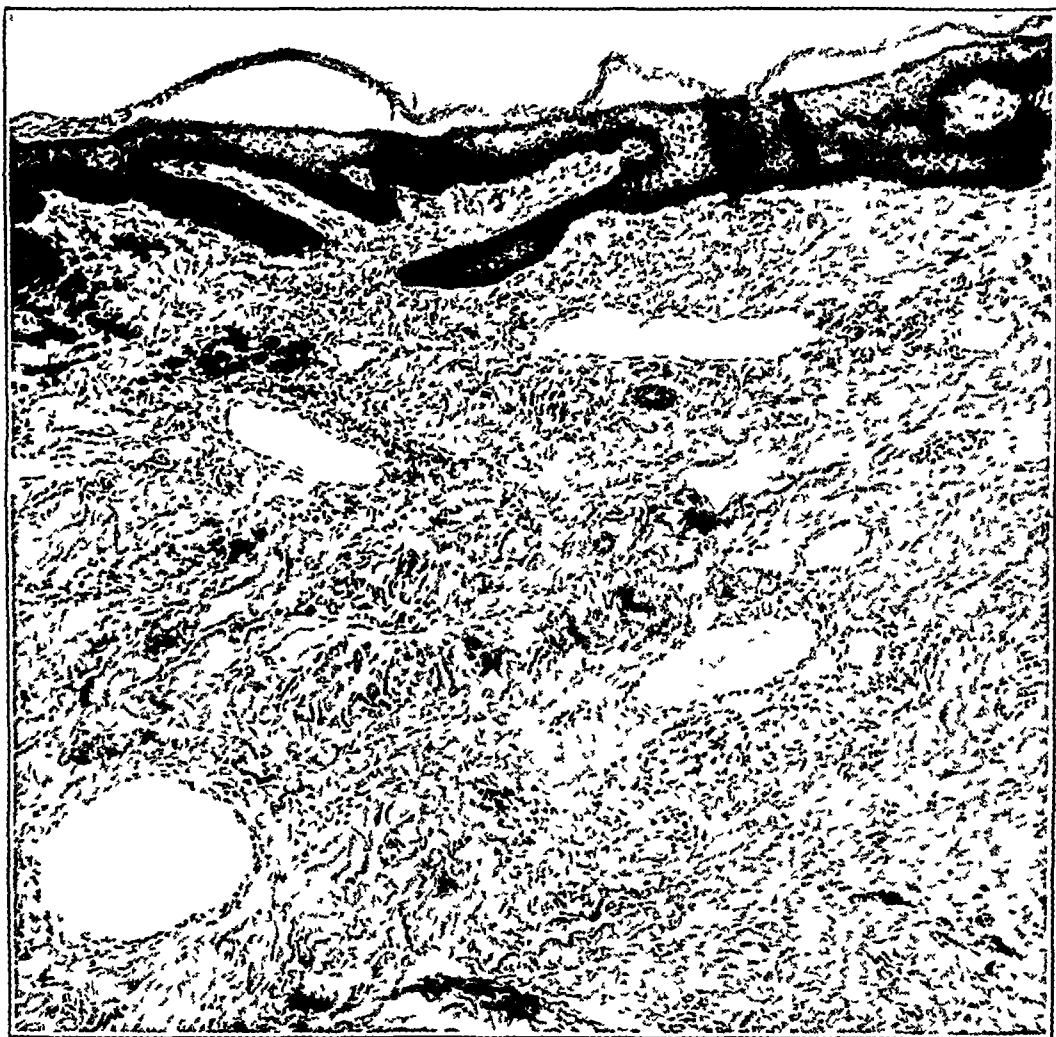


Fig 5—An angioma (low power)

cells of a typical cylindroma, should not be included in this classification. We cannot fully agree with this, although the condition in our case was shown to be not a cylindroma on microscopic examination, its clinical picture was indistinguishable from that seen in the condition. As in our case, in which the growth would also be a nevocarcinoma if a malignant change should occur (malignant development of the junction type nevus), the diagnosis was turban tumor until microscopic examination revealed the true nature of the dermatosis.

In most of the cited cases the tumors seem to be of nevroid origin. This observation also was made by Stillians. In discussing this article, McCarthy corroborated this view, and Weidman furthermore maintained the possible derivation from the skin plate of Remak (an embryologic structure).

Depending on the stage of development the tumors may apparently arise from the epidermis, the sweat glands or the pilosebaceous apparatus. Ronchese¹⁶ was in accord with this view and furthermore suggested that the most probable derivation was from the sebaceous glands. Sutton and Sutton¹⁷ discussed turban tumors under the heading of syringoma but stated the opinion that the origin need not necessarily be from the sweat apparatus but may be from other epithelial structures. In our case, since the tumors were present at birth and the microscopic picture is that of a nevus (mixed), the nature of the dermatosis is evident.

Clinically these cases closely resemble each other, with slight variations. Some had single lesions, others, multiple. Often heredity seemed to play an important role when many members of a family were similarly afflicted. Greater incidence is found among females. At times, in conjunction with the tumors of the scalp, lesions of the face and of the trunk were present. In the reports of Watanabe¹⁸ Schlamadinger,¹⁹ Biberstein²⁰ and others, these tumors proved to be of the trichoepithelioma group.

SUMMARY

The first case of turban tumor in a Negro is reported.

The tumors were present at birth and were confined to the scalp.

The lesions were of mixed, epidermal and dermal types.

Turban tumor is a descriptive clinical term, and in each case histologic study is necessary for diagnosis of the type of nevus.

Dr. David L. Satenstein gave assistance in the preparation of this paper.

921 Bergen Avenue, Jersey City, N. J.

57 West Fifty-Seventh Street, New York.

16 Ronchese, F. Multiple Benign Epithelioma of the Scalp (Turban-Tumors), *Am J Cancer* **18** 875, 1933.

17 Sutton, R. L., and Sutton, R. L., Jr. *Diseases of the Skin*, ed. 10, St. Louis, C. V. Mosby Company, 1939.

18 Watanabe, J. Ueber das Cylindrom und das Epithelioma adenoides cysticum, *Arch f Dermat u Syph* **140** 208, 1922.

19 Schlamadinger, J. Cylindrom und Trichoepithelioma papulosum multiplex, *Arch f Dermat u Syph* **171** 526, 1935.

20 Biberstein, H. Epithelioma adenoides cysticum im Gesicht und Cylindrom am Kopf, *Arch f Dermat u Syph* **142** 428, 1923.

VAGINAL MELANOSIS CAUSED BY BISMUTH THERAPY AND CARCINOMA OF THE CERVIX

KURT WIENER, M D
MILWAUKEE

Discoloration of the skin or mucosa after bismuth medication is known to occur in three forms

1 A general discoloration may be caused by deposits of metallic bismuth in the entire skin, particularly of the face and hands. This extremely rare condition resembles argyria. Lueth, Sutton, McMullen and Muehlberger¹ described and showed a colored picture of a man who for the treatment of a gastric condition took bismuth compounds internally over a long period. He had also taken silver nitrate before. Within a relatively short time his face and hands became deep blue-black, and the covered parts of the body became ashen gray. As in argyria, the discoloration persisted. Chemical analysis of a piece of skin (2 by 4.5 cm) ruled out silver and other metals and gave positive reactions for bismuth. Many small deposits of bismuth were seen in the microscopic sections. Small granules were evenly scattered throughout the corium. Considering the tremendous number of patients treated with bismuth over long periods and the extreme rarity of "bismuthia," one cannot help thinking that one or several unknown factors are essential to produce this spectacular result.

2 Rarely a discoloration follows accidental injection of a bismuth preparation into an artery. There the bismuth salts travel as emboli with the blood stream to the muscles and to the skin, producing acute severe pain and inflammatory reactions, ranging from slight irritation to deep and wide necroses. Most often swelling and purple or bluish net-shaped areas of discoloration are seen. The condition heals, leaving long-lasting pigmentation. Freudenthal,² who in 1924 described the local embolic exanthema due to bismuth, showed in histologic sections that the small arteries in the lesions were filled with crystals identical with those used in the emulsion.

1 Lueth, H. C., Sutton, D. C., McMullen, C. J., and Muehlberger, C. W. Generalized Discoloration of Skin Resembling Argyria Following Prolonged Oral Use of Bismuth. Case of "Bismuthia," *Arch. Int. Med.* **57**: 1115 (June) 1936.

2 Freudenthal, W. Lokales embolisches Bismogenol-Exanthem, *Arch. f. Dermat. u. Syph.* **147**: 155, 1924.

3 The third type of discoloration caused by bismuth is the black deposit of bismuth sulfide. This is the most common form. It has been seen by some authors in more than 90 per cent of the patients treated with injections of a bismuth salt as a narrow gray, blue or black line along the edges of the gums. It appears most frequently in connection with taitai. It is more pronounced on the dental side of the gums than on the buccal side. It usually starts in, and is often confined to, the region of the incisor teeth.

The gum line persists for months after discontinuation of the treatment. In a small number of cases ulcerative or gangrenous stomatitis follows the appearance of the gum line. Oral sepsis and use of soluble bismuth salts accelerate the production of the deposits, which rarely appear in children, in women during the second half of pregnancy (Lohe and Rosenfeld³) or in edentulous mouths (McCarthy and Dexter⁴). Bismuth melanosis of the tongue and of the buccal mucosa is a warning symptom of impending stomatitis and nephritis.

The pathogenesis of the bismuth gum line was investigated soon after the introduction of bismuth in the therapy of syphilis. Similar phenomena were known to occur in cases of occupational lead poisoning and from the use of mercury in the treatment of syphilis. Azoulay,⁵ Biberstein,⁶ Rothman and Kurz,⁷ Lohe and Rosenfeld,³ Der,⁸ Komayo⁹ and many other investigators have made histologic and chemical studies of bismuth impregnation of the gums. The consensus was and still is that the black deposits consist of granules of bismuth sulfide which develop where the soluble bismuth salts, circulating in the blood stream, come in contact with hydrogen sulfide. This gas is formed by bacteria from proteins in decaying organic matter. Taitai and decaying teeth, together with poor dental hygiene, are the most frequent conditions in which a constant development of hydrogen sulfide takes place. There-

3 Lohe, H, and Rosenfeld, H. Wismutpigmentierungen der Blasenschleimhaut, *Dermat Ztschr* **57** 250, 1929.

4 McCarthy, F T, and Dexter, S O, Jr. Oral Manifestations of Bismuth, *New England J Med* **213** 345, 1935.

5 Azoulay, R. Stomatite bismuthique, *Presse med* **30** 134, 1922, abstracted, *Zentralbl f Haut- u Geschlechtskr* **5** 255, 1922.

6 Biberstein, H. Ueber die Wismutbehandlung des Syphilis, *Deutsche med Wchnschr* **49** 1518, 1923.

7 (a) Rothman, S, and Kurz, R. Ueber den Chemismus des Wismutsaumes, *Klin Wchnschr* **5** 943, 1926, (b) Chemische Untersuchungen ueber Wismutstomatitis, abstracted, *Zentralbl f Haut- u Geschlechtskr* **20** 232, 1926.

8 Der, O. Entstehung und Histologie des Wismutsaumes, *Gyogyaszat* **66** 25, 582, 1926, abstracted, *Zentralbl f Haut- u Geschlechtskr* **21** 509, 1927.

9 Komayo, G. Ueber eine histochemische Nachweismethode der Resorption, Verteilung und Ausscheidung des Wismuts in den Organen, *Arch f Dermat u Syph* **149** 277, 1925.

fore, bismuth sulfide is formed in the mouth almost regularly during bismuth medication. But hydrogen sulfide is not only formed in the oral cavity. It is constantly present in the colon. It is here that one should also expect bismuth melanosis. However, there have been sufficient postmortem examinations of bismuth-treated syphilitic patients to show that bismuth melanosis in the colon is extremely rare. Micsch¹⁰ observed 2 cases of black discoloration involving the large intestine from the ileocecal valve to the anus. In these cases the typical granula-



Fig 1—Vaginal melanosis. Notice the fine black dots (papillae) on the vulva. The black area in the center of the picture is not shadow but black discoloration of the vaginal mucosa.

tion and reactions due to bismuth sulfide were seen mainly in the capillary endothelial cells of the upper strata of the connective tissue. The condition in these cases was well differentiated from other pigmentations of the colon, e. g. Pick's melanosis. Jadassohn¹¹ observed

10 Micsch, G. Wismut-Melanose der Dickdarmschleimhaut, Beitr z path Anat u z allg Path **92** 147, 1933.

11 Jadassohn, J., in discussion on Muller, H., and Blass. Demonstration zur Wismutbehandlung, Arch f Dermat u Syph **145** 348, 1924.

a case of complete melanosis of the oral mucosa. Lohe and Rosenfeld³ observed bismuth melanosis of the urinary bladder. Black smegma and black margins in infected tonsils during bismuth treatment are known.

In spite of the fact that decaying organic matter is present in the uterus or vagina under many conditions, melanosis of the vagina seems to be as rare as melanosis of the colon. As far as I know, no cases have been reported as yet. In the many syphilitic patients who were receiving injections of a bismuth preparation and simultaneous vaginal treatment for purulent or ulcerative conditions (gonorrhea, cervicitis), I have never seen melanosis of the vagina. I therefore feel justified in presenting the following cases.

REPORT OF A CASE

Mrs. X. Y., a white woman aged 30, was referred to me for radiation therapy of cancer of the cervix on Jan. 18, 1939. She had been bleeding since about June



Fig. 2—Bismuth deposits (black lines) in the gums

1938. A large cauliflower growth had been removed from the cervix in January 1939. From January 18 to February 28 the patient was treated with high voltage roentgen rays in protracted and fractional doses. A total of 6,800 r filtered through 0.5 and 1 mm of copper at 200 kilovolts, 15 milliamperes and 50 cm distance was given through five portals. There was a moderate reaction of the skin, which healed with dry scaling. This course was followed by treatment of the cervix with radium from April 4 to April 8. A dose of 3,070 milligram hours was given by means of tubes placed in the cervical crater. The filtration was 15 mm of brass plus 0.3 mm of platinum. There was a good response. The crater became clean and small. The patient was in excellent general condition and gained much weight.

But in September she started complaining about pain in the back and vaginal discharge. The crater was larger again and had hard, infiltrated edges and a necrotic floor. The vaginal mucosa was normal. A new course, of 3,000 r, high voltage roentgen rays was given from September 9 to September 29. At an examination on this day the vagina appeared black. There was still a large necrotic crater of the cervix, with much foul discharge, but the vaginal mucosa seemed normal except for its color. The condition looked much like a submucosal

hemorrhage, but no cause for such a large extravasation could be discovered. Until November 20 no change in the color of the vagina took place.

The patient had a syphilitic infection of unknown duration. She had Argyll Robertson pupils and a 4 plus Kahn reaction of the blood. She had received a total of 83 cc of a preparation of basic bismuth salicylate (bismogenol), yielding 4.15 Gm of bismuth, from Oct 29, 1938, to Nov 10, 1939. These injections were given at intervals of approximately five days, in conjunction with liver extract (Dr Decker). This treatment was well tolerated.

In November 1939 the patient had a black linear deposit of bismuth along the gums and black spots and dots (papillae) on the edges of the tongue corre-



Fig 3—Bismuth deposits in the papillae and in the superficial submucous connective tissue (hematoxylin and eosin, low power)

sponding to the interdental spaces. There were many deposits of tartar and decayed and filled teeth.

The vaginal mucosa was still almost entirely velvety black. There were only a few small areas of lighter color crossed by black lines, corresponding to the columnae rugarum. There were some areas of slightly black discoloration around the urethral orifice and some fine black points on both sides of the vulva, probably corresponding to papillae.

The rectal mucosa was of normal appearance. A specimen of tissue was taken from the edge of the black area in the posterior vaginal wall and prepared for histologic study in Mount Sinai Hospital.

Histologic Examination—The vaginal epithelium was normal. The underlying submucosa showed slight increase of cells, mainly lymphocytes. The papillae were mostly slender. Groups of them contained black bodies, apparently the

deposits of bismuth. They consisted of black amorphous granules, which were mainly accumulated within endothelium cells. This is particularly true of cells in some papillae. Some small but black granules were found in intercellular spaces. There was little inflammatory reaction, hardly more than in areas containing none or scarcely any bismuth.

The patient has never been exposed to or given treatment with metal salts, which are liable to produce melanosis, particularly silver and lead. Owing to



Fig 4—The deposit in the papillae consists of cell-shaped bodies, which apparently are endothelial cells impregnated with bismuth sulfide (high power)

the history of the orally administered bismuth compound and deposits of the same color, together with the history of long and intensive bismuth therapy, it seemed most likely that the melanosis was caused by bismuth sulfide. To prove this several histochemical reactions were performed.

1 Komayo's reaction (modification of Leger's method). The deparaffinized sections were stained with a mixture of 2 per cent quinine sulfate solution and 4 per cent potassium iodine solution, to which some drops of nitric acid had

been added After a minute, the sections were quickly washed in weak nitric acid, dehydrated and counterstained with gentian violet The deposits in the sections showed bright yellow halos This reaction is supposed to be specific for bismuth deposits

2 The sections were treated with hydrogen peroxide, which decolorized the black-brown granules almost completely The color came back after the sections were exposed to freshly developed hydrogen sulfide for five to twenty minutes Then the deposits appeared black, darker than they had been before

COMMENT

Bismuth melanosis, the pathogenesis of which is supposed to be "completely plain,"¹² still has its problems Why does it rarely occur in other areas than in the mouth? Why is it seen in the colon so rarely, in spite of the constant formation of hydrogen sulfide there? Which factors cause the unusual impregnation with bismuth sulfide in some cases, while no melanosis is observed in many similar cases?

SUMMARY

The various types of melanosis caused by bismuth medication are reviewed A case is described in which bismuth melanosis of the entire vagina occurred in a syphilitic patient with an ulcerative cervical cancer

Technical assistance was given by Dr N Enzer, Director of Laboratories of Mount Sinai Hospital, and by his staff, especially Miss A Leininger and Miss G Ballard Mr L C Massopust, Marquette Medical School, made the photomicrographs Dr H G Decker referred the patient to me and permitted the publication of the case

12 Juliusberg, F Die Nebenwirkungen der Wismutbehandlung, in Jadassohn, J Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol 18, p 441

RELAPSING EARLY ACUTE ARSENICAL ERYTHEMA

REPORT OF TWO CASES

EVAN W THOMAS, M D

AND

ORLANDO CAÑIZARES, M D

NEW YORK

In a recently published article¹ we reported 11 cases of early acute arsenical erythema. In that article we stated that "Not a single recurrence of exactly this type of reaction has ever been reported." Gastrointestinal disturbances and nitritoid crises seemed to be the most common complications when arsphenamine therapy was resumed.

Since then we have observed 2 cases in which the symptoms characterizing early acute arsenical erythema reappeared one or more times with the resumption of injections of arsenic. Fever, eruptions and adenitis and in 1 case conjunctivitis and punctate keratitis occurred after treatment with arsenicals was resumed. The intensity of these reactions decreased with the number of injections, and administration of the drugs was not permanently stopped because of them.

Further search of the literature shows that Milian² himself admitted the possibility of a recurrence of the "erythema of the ninth day." He stated that the recurrence takes place chiefly in patients with erythema multiforme eruptions. The behavior in our 2 cases suggests a close relation between this type of eruption and the so-called "toxic eruptions" due to other drugs. Because of the unusual features presented by 1 of our cases a detailed report may be of interest.

REPORT OF CASES

CASE 1—C F, a Negress aged 22, was admitted to Bellevue Hospital on Feb 24, 1939, with a generalized maculopapular rash diagnosed as secondary syphilis. The Wassermann reaction of the blood was strongly positive, although it had been negative six weeks earlier when her husband was found to have secondary syphilis. She was included in a series of patients with early syphilis.

From the Department of Dermatology and Syphilology, New York University College of Medicine, and the Department of Dermatology and Syphilology, Third Medical Division (New York University), Bellevue Hospital, service of Dr Edward R. Maloney.

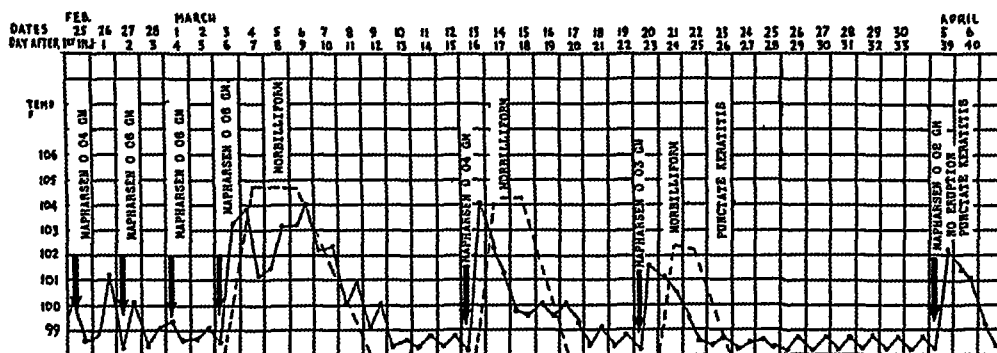
1 Cañizares, O., and Thomas, E. W. Early Acute Arsenical Erythemas, *Arch Dermat & Syph* 39 867-876 (May) 1939.

2 Milian, G. Les érythèmes interthérapeutiques du neuvième jour, *Bull Acad de méd, Paris* 109 704-711 (May) 1933.

who were given injections of mapharsen three times a week for the first four weeks of their treatment

On February 25 she received 0.04 Gm of mapharsen, without difficulty. On February 27 she received 0.06 Gm. On March 1 and 3 she was again given 0.06 Gm, with no immediate reaction. On the evening of March 3, seven days after the first injection and about twelve hours after the fourth, her temperature rose to 103.8 F. This was preceded by a chill and was associated with nausea and vomiting. She had no sore throat, but the following day a generalized erythema was noted and the conjunctivas of both eyes were injected. She also had some photophobia and increased lacrimation. She had several slightly tender cervical nodes. The fever lasted five days, and the erythema was entirely gone in four days.

No further treatment was attempted until five days after her temperature had become normal. On March 13 she received 0.04 Gm of mapharsen, which was followed within a few hours by a rise in temperature to 104 F. Nausea and vomiting started about two hours after the injection. On the following morning she again had a generalized erythema, which was entirely macular and consisted of red blotches. Her conjunctivas were injected, and photophobia was present. Her throat was not sore, but she had a "strawberry" tongue, with bright red raised



Temperature chart for C. F., a Negress aged 22. Dotted line indicates intensity and duration of rash.

papillae. Within two days the condition on the tongue and the rash cleared up, but she continued to complain of nausea and generalized aches and pains for another two days.

On March 21 she was given 0.02 Gm of mapharsen, which was followed by nausea and vomiting and a rise in temperature to 101.4 F. The following day she again had a generalized erythematous blotchy rash. There was less injection of her conjunctivas than on the two previous occasions, but she complained of pain in her eyes and cloudiness of vision. Examination revealed superficial punctate keratitis, confirmed by consultation with the ophthalmic service. The fever and eruption lasted for less than two days, but the keratitis remained for ten days.

On April 5 she was given 0.02 Gm of mapharsen. Her temperature rose that evening to 102.4 F. No eruption occurred, but she had mild conjunctivitis, associated with punctate keratitis, which lasted for five days.

On April 13 and 22 she was given 0.02 Gm of mapharsen with 8 minims (0.49 cc) of epinephrine hydrochloride (1 to 1,000 dilution). She had slight and brief rises in temperature on both occasions but no rash, nausea or vomiting. Her eyes, however, showed slight keratitis for several days after each injection.

On April 25 she was given 0.3 Gm of acetylglucoarsphenamine intramuscularly, with no reaction. This was followed by eight injections of bismuth subsalicylate

in the outpatient department Mapharsen was then tried again in doses of 0.01 Gm, without experiencing any difficulty. The dose was increased gradually to 0.06 Gm. She now has a negative Wassermann reaction of the blood and is continuing her treatment without difficulty. The ophthalmic service has reported that both corneas are normal. Treatment with mapharsen was resumed only after all symptoms and the superficial keratitis had subsided. Slit lamp examinations at no time revealed anything resembling interstitial keratitis.

CASE 2—A Chinese man aged 60 was admitted to Bellevue Hospital with secondary syphilis. He was treated with neoarsphenamine, starting with 0.3 Gm. Seven days after his first injection and one day after the second, fever developed, with a temperature of 103 F. On the following day he had a generalized scarlatiniform rash and a sore throat. Four days after the disappearance of all symptoms he was again given neoarsphenamine, which was followed by another scarlatiniform eruption which lasted only for about twenty-four hours. His temperature rose to 102 F but became normal within two days. Subsequent injections of the same drug were well tolerated.

THE USE OF SULFANILAMIDE IN DERMATOLOGY

RAYMOND P HUGHES, M D

EL PASO, TEXAS

The introduction of sulfanilamide to the medical profession in 1936 has brought about many changes in therapy in practically every field of medicine. Probably there is no field or specialty in which its value has not been tested clinically as well as experimentally in the laboratory. Nor is there any field in which its value has not been proved as a decided aid to therapy of conditions for which there has been heretofore no valuable remedy.

With the introduction of any new effective drug there is a tendency to extend its use more or less promiscuously. Such spectacular results were obtained with sulfanilamide in many cases of streptococcic infections that it was soon used for all recalcitrant ailments. Its improper use was partly due to the popular belief at the outset that the drug was harmless and did not cause any untoward manifestations. This practice precipitated a large number of untoward and serious reactions, which in turn have caused a wave of skepticism among both patients and physicians. This is unfortunate, because many patients for whom the drug is indicated are denied its benefits owing to a false fear on the part of the physician or of the patient himself.

The purpose of this communication is to present an unbiased evaluation of sulfanilamide in the field of dermatology.

Domagk¹ in 1935 reported favorable therapeutic effects on hemolytic streptococcic infections in mice from the use of a dye (the hydrochloride of 4-sulfamido-2',4'-diaminoazobenzene) which was called prontosil. Later another substance (disodium 4-sulfamidophenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3'-6'-disulfonate) was introduced; this was known as prontosil soluble or prontosil S and later as prontosil and as neoprontosil and recently has been given the nonproprietary name azo-sulfamide. Tréfouël, Tréfouël, Nitti, Nitti and Bovet² found that the action of these two preparations was due to a common breakdown

From the Clinics of Leslie M. Smith, M D, and Raymond P. Hughes, M D.

Thesis submitted to the Faculty of the Graduate School of Medicine of the University of Pennsylvania, in partial fulfillment of the requirements for the degree of Master of Medical Science (M. S. [Med.]) for graduate work in dermatology and syphilology.

1 Domagk, G. *Deutsche med. Wchnschr.* **61** 250, 1935.

2 Tréfouël, J., Tréfouël, J. (Mme.), Nitti, J., Nitti, F., and Bovet, D. *Compt. rend. Soc. de biol.* **120** 756, 1935.

product This substance was paraaminobenzenesulfonamide, to which the name sulfanilamide was applied by the Council on Pharmacy and Chemistry of the American Medical Association

The exact mode of action of sulfanilamide is not yet understood According to Keefer,³ the following suggestions have been offered as to its action 1 It is a bacteriostatic agent 2 It stimulates phagocytosis 3 It neutralizes bacterial toxins 4 It is bactericidal under certain conditions 5 It delays growth of organisms until mononuclear phagocytes accumulate 6 It alters organisms so that phagocytosis can take place From the work of Bliss and Long⁴ and Keefer and Rantz,⁵ it is evident that at least in hemolytic streptococcal infections the action of sulfanilamide is bacteriostatic

Since the early work sulfanilamide has been found of definite value in a number of infections caused by a variety of organisms Only the conditions related to dermatology are within the scope of this paper

From the standpoint of convenience and effectiveness sulfanilamide is probably best administered orally in tablet form Although the drug is soluble in water only to a small degree (0.8 per cent) and is only slightly absorbed in the stomach, the absorption from the small intestine is rapid and definite⁶ In patients who are unable to swallow or who are unable to retain the drug owing to nausea, the injectable form of sulfanilamide is of course preferable To accelerate absorption when administration of the drug is begun a large volume of water should be given When the proper concentration of the compound in the blood is reached, however, it is well to restrict the fluid intake in order to help maintain this level Sulfanilamide is eliminated almost entirely by the kidneys⁷ As yet there is no safe solvent for sulfanilamide except water

To a large degree the success obtained from the administration of sulfanilamide is dependent on the promptness with which the proper concentration in the tissues and in the blood is reached and the maintenance of this concentration According to Long, Bliss and Feinstein⁷ a blood concentration of from 10 to 15 mg per hundred cubic centimeters is indicated for severe infections For mild or moderately severe infections a blood concentration of from 5 to 10 mg per hundred cubic centimeters is probably sufficient Keefer³ stated that from 7 to 10 mg

3 Keefer, C S *New England J Med* **219** 562, 1938

4 Bliss, E A, and Long, P H *Observations on Mode of Action of Sulfanilamide*, *J A M A* **109** 1524 (Nov 6) 1937

5 Keefer, C S, and Rantz, L A, cited by Keefer³

6 Marshall, E K, Jr, Cutting, W C, and Emerson, K, Jr *Toxicity of Sulfanilamide*, *J A M A* **110** 252 (Jan 22) 1938

7 Long, P H, Bliss, E A, and Feinstein, W H *Mode of Action, Clinical Use and Toxic Manifestations of Sulfanilamide Further Observations*, *J A M A* **112** 115 (Jan 14) 1939

per hundred cubic centimeters is adequate for most infections. In order to establish and maintain these levels in the blood and tissue there is some question as to the size of dosage and as to the frequency with which the drug should be given. The time between doses has been shortened greatly during the past few months. At first the drug was given at six and eight hour intervals, whereas now it is most frequently given at four hour intervals. Possibly in the future it will be learned that the interval should be shortened still more in order to keep the blood and tissue fluids supplied with fresh sulfanilamide. Keefer³ and Long, Bliss and Feinstone⁷ began treatment with approximately 60 mg per kilogram ($\frac{1}{2}$ grain per pound) of body weight as the initial dose. They then continued with about 15 to 20 mg per kilogram ($\frac{1}{10}$ to $\frac{3}{25}$ grain per pound) of body weight at four hour intervals. As the drug is excreted rapidly it is most important to give it at regular four hour intervals, both day and night, in order to maintain an adequate concentration in the blood and in the tissues.

The question as to the duration of the treatment is of considerable importance and has not as yet been definitely settled. When the drug was first introduced it was the idea of many that its administration should not be continued longer than a few days. Most writers now, however, have agreed that the period of administration may safely be lengthened when indicated. Long, Bliss and Feinstone⁷ now prefer to give the drug until the patient has practically recovered and with some purulent infections to continue administration for at least ten days after the patient is well. This will assure fewer recurrences.

Most authorities agree that it is not advisable to administer saline cathartics during the course of sulfanilamide therapy. No other drugs seem to be contraindicated. In fact, when other drugs are indicated they should be given along with sulfanilamide. Alcohol should be forbidden, as it has a tendency to accentuate the cerebral symptoms.

Long and Bliss⁸ recommended the administration of sodium bicarbonate at all times to combat acidosis. In 1937 Southworth⁹ called attention to the fact that patients receiving sulfanilamide had a fall in the carbon dioxide-combining power of the plasma which he interpreted as indicating an acidosis. The investigations of Hartmann, Perley and Barnett,¹⁰ on the other hand, seem to prove that the usual disturbance in the acid-base balance produced by sulfanilamide is actually an alkalosis.

The clinical use of sulfanilamide has resulted in a rather wide variety of toxic manifestations.⁷ With the continued use of the product there

8 Long, P. H., and Bliss, E. A. *South M J* **30** 479, 1937

9 Southworth, H. *Proc Soc Exper Biol & Med* **36**.58, 1937

10 Hartmann, A. F., Perley, A. M., and Barnett, H. L. *J Clin Investigation* **17**:465, 1938

seems to be a growing list of toxic features which have not been manifest previously. In experimental animals the toxicity is low,¹¹ but toxic symptoms of some degree are demonstrable in a large number of human beings treated. Fortunately, by far the large majority of these are harmless and are relieved by withdrawal of the drug, and few have been reported which are severe and definitely dangerous.

MILD REACTIONS

Among the acute toxic reactions of a milder nature observed after the administration of sulfanilamide to man are fever, anorexia, cyanosis, nausea, vomiting, dizziness, mental confusion and excitement. These, when they occur, usually come on within a short time after the first dose is given. Although not dangerous, they are often alarming to both patient and physician if they are not aware of the likelihood of their occurrence. Rarely in my experience have such manifestations been severe enough to warrant discontinuance of administration of the drug. Long, Bliss and Feinstein⁷ expressed the opinion that when graver complications develop they are preceded soon after the administration of the drug by fever, which is consequently to be regarded as a danger sign. They recommended discontinuance of administration of the drug when an unexplained fever develops. Sulfanilamide fever usually develops between the fifth and the tenth day of treatment.

The mechanism of cyanosis during the administration of sulfanilamide is as yet unexplained. Marshall and Walzl¹² expressed the opinion that the formation of methemoglobin is always responsible for the cyanosis. It is not regarded as a serious complication, however, and does not warrant discontinuance of the treatment.

Most of the other minor symptoms are thought to be of cerebral origin and in the majority of instances will disappear or become much less annoying within twenty-four to forty-eight hours. With ambulatory patients who must attend to active and exacting duties there is occasionally necessity for withdrawal of the drug on this account.

MAJOR COMPLICATIONS

Of the serious or major complications resulting from the use of sulfanilamide, probably the most common is anemia. It occurred in 4 per cent of a series of over 500 patients treated in Johns Hopkins Hospital.¹³ Price and Myers¹⁴ reported its occurrence in 5 per cent

11 Bieter, R. N. *Journal-Lancet* 59 139, 1939.

12 Marshall, E. K., Jr., and Walzl, E. M. *Bull. Johns Hopkins Hosp.* 61 140, 1937.

13 Wood, W. B. *Anemia During Sulfanilamide Therapy*, J. A. M. A. 111 1916 (Nov. 19) 1938.

14 Price, A. E., and Myers, G. B. *Treatment of Pneumococcic Pneumonia with Sulfanilamide*, J. A. M. A. 112 1021 (March 18) 1939.

of a series of 115 cases. It usually appears in twenty-four to seventy-two hours after the onset of medication, and the earliest signs are those of jaundice. Wood¹⁵ has reported 1 death from hemolytic anemia. If administration of the drug is discontinued and the proper steps are taken, recovery almost invariably occurs.

Jaundice is a common toxic symptom which necessitates withdrawal of the drug. It is usually hemolytic but occasionally is due to hepatic damage. Cline¹⁶ has reported 1 case of acute yellow atrophy of the liver following administration of sulfanilamide.

Neuritis is an extremely rare toxic manifestation. Bucy¹⁷ reported 1 case of optic neuritis which gradually cleared up after administration of the drug was discontinued.

Agranulocytosis is a rare but probably the most serious of all complications and is usually fatal. Death occurs within two or three days after the onset of the agranulocytosis. Kracke¹⁸ has collected 9 cases which occurred as a result of sulfanilamide therapy. A few others who have reported cases are Ballenger,¹⁹ Culbreath,²⁰ Johnston,²¹ Jones and Miller²² and Long and Bliss.²³ The condition rarely develops until the patients have taken the drug for two weeks or longer. Myers²⁴ stated the belief that there is little danger of this complication developing if warning signs, such as fever and dermatitis, are heeded.

CUTANEOUS REACTIONS

Since the first use of sulfanilamide there have been numerous reports of varying types of cutaneous toxic reactions. Long, Bliss and Feinstein⁷ reported dermatitis occurring as a complication in 1.6 per cent of his patients, while Hageman and Blake²⁵ reported its occurrence in as many as 15 per cent of all patients they had treated.

The usual eruption is morbilliform, although several other types have been reported. Among the first to report a toxic cutaneous reaction

15 Wood, H. *South M J* **31** 646, 1938.

16 Cline, E. W. *Acute Yellow Atrophy of Liver Following Sulfanilamide Medication*, *J A M A* **111**:2384 (Dec 24) 1938.

17 Bucy, P. C. *Toxic Optic Neuritis Resulting from Sulfanilamide*, *J A M A* **109**:1007 (Sept 25) 1937.

18 Kracke, R. R. *Relation of Drug Therapy to Neutropenic States*, *J A M A* **111** 1256 (Oct 1) 1938.

19 Ballenger, H. C. *Ann Otol, Rhin & Laryng* **46**:1129, 1937.

20 Culbreath, P. H. *J South Carolina M A* **34**:307, 1938.

21 Johnston, F. D. *Lancet* **2** 1044, 1938.

22 Jones, H. W., and Miller, C. P. *J Lab & Clin Med* **24**:121, 1938.

23 Long, P. H., and Bliss, E. A. *Canad M A J* **37**:457, 1938.

24 Myers, G. B. *J Michigan M Soc* **38**:302, 1939.

25 Hageman, P. D., and Blake, F. G. *Specific Febrile Reaction to Sulfanilamide*, *Drug Fever*, *J A M A* **109**:642 (Aug 28) 1937.

to the drug were Newman and Shailit,²⁶ who reported 4 cases of eruptions in areas exposed to sunlight. They were able to reproduce the same type of reaction on other surfaces by exposure to ultraviolet irradiation. Menville and Archinard²⁷ reported a series of 4 cases of reactions also on exposed surfaces after administration of the drug. Frank²⁸ reported 2 cases in which the eruption was more pronounced on the surfaces exposed to sunlight, but lesions of erythema multiforme were also present on covered surfaces of the body. Goodman and Levy²⁹ reported 2 cases of a maculopapular generalized eruption occurring after small doses of sulfanilamide were taken, in 1 of which a scratch test with the drug gave a positive reaction. Salvin³⁰ reported a case of dermatitis due to sulfanilamide in which there was a positive reaction to patch tests and in which a small dose caused a recurrence of the dermatitis. Schwentker and Gelman³¹ in a series of 180 cases reported a morbilliform eruption in 6 per cent of cases, in which fever and malaise always accompanied the eruption. The eruption was usually generalized. Finney³² reported a case of severe itching and edema of the face, arms and chest accompanied by a generalized maculopapular eruption. There was moderate elevation of temperature. Schlesinger and Mitchell³³ studied 10 cases of sulfanilamide dermatitis and noted the syndrome of prodromal fever and a morbilliform eruption occurring most commonly on the ninth day in all cases and splenomegaly in many. Feldman³⁴ and DeOreo³⁵ both reported cases in which scarlatiniform eruptions developed on the covered surfaces of the body after three weeks' treatment (Feldman) and after two days' administration of the

26 Newman, B. A., and Shailit, H. Sulfanilamide Photosensitizing Agent of Skin, *J. A. M. A.* **109** 1036 (Sept 25) 1937

27 Menville, J. G., and Archinard, J. J. Skin Eruptions in Patients Receiving Sulfanilamide. Report of Four Cases, *J. A. M. A.* **109** 1009 (Sept 25) 1937

28 Frank, L. J. Dermatitis from Sulfanilamide, *J. A. M. A.* **109** 1011 (Sept 25) 1937

29 Goodman, M. H., and Levy, C. S. Development of Cutaneous Eruption (Toxicodermatosis) During Administration of Sulfanilamide. Report of Two Cases, *J. A. M. A.* **109** 1009 (Sept 25) 1937

30 Salvin, M. Hypersensitivity to Sulfanilamide, *J. A. M. A.* **109** 1038 (Sept 25) 1937

31 Schwentker, F. F., and Gelman, S. *Bull. Johns Hopkins Hosp.* **61**, 136, 1937

32 Finney, J. O. Severe Dermatitis Medicamentosa Following Administration of Sulfanilamide, *J. A. M. A.* **109** 1982 (Dec 11) 1937

33 Schlesinger, E. R., and Mitchell, W. L., Jr. Sulfanilamide Eruption. Study of Patients with Morbilliform Rash and of Their Subsequent Reactions, *Am. J. Dis. Child.* **56** 1256 (Dec) 1938

34 Feldman, S. Pemphigus Treated with Sulfanilamide. Sulfanilamide Eruption, *Arch. Dermat. & Syph.* **39** 601 (March) 1939

35 DeOreo, G. A. Dermatitis Medicamentosa from Sulfanilamide, *Arch. Dermat. & Syph.* **40** 332 (Aug) 1939

drug (DeOreo) Loveman and Simon³⁶ reported a case of fixed eruption accompanied by stomatitis following ingestion of the drug. The symptoms subsided on withdrawal of the drug and were reproduced when it was given again. Patch tests gave negative results on unaffected areas but positive results on previously affected skin. Noun³⁷ also reported a case with lesions of the mucous membranes accompanying an urticarial type of eruption. Schonberg³⁸ reported a case in which a purpuric eruption developed after four days' treatment with the drug. A few weeks later the patient was given 5 grains (0.32 Gm) of sulfanilamide and a generalized scarlatiniform eruption and high fever developed. Cleveland³⁹ reported a case of varioliform eruption following the use of sulfanilamide. The eruption was not confined to the exposed surfaces, and some of the lesions resembled erythema multiforme. There was no itching, and the pustules did not produce any scarring. Costello⁴⁰ presented a case in which lupus erythematosus developed for the first time about three months after the patient had been given sulfanilamide for a vaginal infection. The eruption appeared over exposed areas after severe sunburn. Bettley and Simon⁴¹ reported a case of bullous eruption occurring after the administration of sulfanilamide. The patient first presented a morbilliform rash accompanied by malaise, nausea and vomiting. Administration of the drug was continued, and several days later a bullous type of eruption appeared on the exposed surfaces after exposure to sunlight. Myers, Vonder Heide and Balcerski⁴² reported on exfoliative dermatitis in a patient who had taken sulfanilamide for twenty-eight days. It was accompanied by purpura, fever and transient jaundice. The condition had started with a morbilliform eruption. A positive reaction to a patch test caused a flare-up in the dermatitis.

To summarize, the following types of cutaneous reactions have been reported in the literature: morbilliform eruption, dermatitis from photosensitization, erythema multiforme, scarlatiniform eruption, fixed eruption, stomatitis, urticaria, purpura, varioliform eruption, and exfoliative dermatitis.

36 Loveman, A. B., and Simon, F. A. Fixed Eruption and Stomatitis Due to Sulfanilamide, *Arch. Dermat. & Syph.* **40**:29 (July) 1939.

37 Noun, M. H. Erosions of Oral Mucosa and Urticaria of Body Following Small Doses of Sulfanilamide, *Arch. Dermat. & Syph.* **37**:1045 (June) 1938.

38 Schonberg, I. L. Purpuric and Scarlatiniform Eruption Following Sulfanilamide, *J. A. M. A.* **109**:1035 (Sept. 25) 1937.

39 Cleveland, D. E. H. Varioliform Eruption from Sulfanilamide, *Arch. Dermat. & Syph.* **39**:693 (April) 1939.

40 Costello, M. Lupus Erythematosus Precipitated by Sunlight After Sulfanilamide Therapy, *Arch. Dermat. & Syph.* **39**:598 (March) 1939.

41 Bettley, F. R., and Simon, P. *Brit. M. J.* **1**:1177, 1939.

42 Myers, G. B., Vonder Heide, E. C., and Balcerski, M. Exfoliative Dermatitis Following Sulfanilamide, *J. A. M. A.* **109**:1983 (Dec. 11) 1937.

In my own experience I have observed 6 cases of generalized maculopapular or morbilliform eruption, 4 cases of erythema multiforme, 2 of urticaria, 3 cases of a papular dermatitis of the face, neck, forearms and hands following exposure to sunlight, 1 of scarlatiniform eruption and 1 of exfoliative dermatitis. All of these eruptions disappeared promptly on discontinuance of administration of the drug with the exception of the exfoliative dermatitis. This condition was generalized and severe and has been present for several months, without any tendency to disappear in spite of thorough treatment by several competent dermatologists in different parts of the country.

SULFANILAMIDE FOR DERMATOLOGIC CONDITIONS, REVIEW OF THE LITERATURE

Sulfanilamide has been used in the treatment of a large number of dermatologic conditions, with varying degrees of success. As yet there is considerable difference of opinion concerning its value against most cutaneous diseases, but this is natural in view of the fact that it is still a new drug and time has not permitted sufficient trial or sufficient observation after its use for a unanimity of opinion to be established. Realization of its proper value will come only as a result of several years' experience and with the exchange of ideas over different parts of the country.

Probably one of the most common uses of sulfanilamide in the field of dermatology is that of the treatment of lupus erythematosus. Ingels⁴³ reported 5 cases. All 5 patients were greatly improved, and 2 were apparently completely cured. Sulzberger⁴⁴ reported on 3 patients with the subacute discoid type of lupus erythematosus. All were greatly improved by the treatment. Other treatment tried previously in the same cases had failed. Abramowitz⁴⁵ reported the cure of 3 patients with acute disseminate lupus erythematosus. He stated that he had never before seen this condition cured by other methods of therapy. Belote⁴⁶ described 2 patients who had been desperately ill with acute lupus erythematosus but who were at the time of his report in a state of remission after treatment with sulfanilamide. Anderson⁴⁷ reported

43 Ingels, A. E. Lupus Erythematosus Treated with Sulfanilamide, *Arch Dermat & Syph* **37** 879 (May) 1938.

44 Sulzberger, M. B. Lupus Erythematosus Treated with Sulfanilamide, *Arch Dermat & Syph* **39** 610 (March) 1939.

45 Abramowitz, E. W., in discussion on Wise, F. Discoid Lupus Erythematosus Undergoing Dissemination, *Arch Dermat & Syph* **38** 661 (Oct) 1938.

46 Belote, G. H. Lupus Erythematosus Disseminatus, *Arch Dermat & Syph* **39** 793 (May) 1939.

47 Anderson, H. F. Fulminating Acute Lupus Erythematosus Cured by Sulfanilamide, *Arch Dermat & Syph* **38** 621 (Oct) 1939.

on a patient with fulminating acute lupus erythematosus who had remained cured for six months after sulfanilamide had been given. The condition was precipitated by the administration of gold sodium thiosulfate. Lindsay⁴⁸ reported a case of acute lupus erythematosus in which the eruption had been aggravated by gold therapy. The patient improved greatly from sulfanilamide treatment until a dermatitis developed from the sulfanilamide, at which time its administration was discontinued. She remained free of eruption for two months and then had a recurrence. Sulfanilamide was given again, after which the condition cleared completely, without ill effects from the drug. Wollenberg⁴⁹ reported a case of acute disseminated lupus erythematosus which had been extremely resistant to treatment of all types. After the administration of sulfanilamide the condition cleared promptly. Wilson,⁵⁰ on the other hand, had a patient with typical acute disseminated lupus erythematosus from the lesions of which a streptococcus was cultured. After well controlled treatment for twelve days the patient failed to show any improvement and died. Jamieson⁵¹ also reported a case of lupus erythematosus disseminatus of four years' duration which showed no response to sulfanilamide and likewise failed to improve with other types of treatment.

Bregman⁵² observed a case of erythema multiforme in which sulfanilamide had a definite curative effect. Benefit was noted after twenty-four hours.

Eller⁵³ treated a patient with pemphigus with sulfanilamide and obtained moderate relief. Caro⁵⁴ reported great improvement in 2 cases of pemphigus. Lain and Lamb⁵⁵ obtained a spectacular cure of a "pemphigoid" eruption. There had been no recurrence at the time of the report, four weeks later.

48 Lindsay, H. C. L. Lupus Erythematosus, *Arch Dermat & Syph* **39**: 888 (May) 1939.

49 Wollenberg, R. A. C. Lupus Erythematosus Disseminatus, *Arch Dermat & Syph* **38**:295 (Aug) 1938.

50 Wilson, J. F. Sulfanilamide in Treatment of Acute Lupus Erythematosus, *Arch Dermat & Syph* **40**:241 (Aug) 1939.

51 Jamieson, R. C. Lupus Erythematosus Disseminatus, *Arch Dermat & Syph* **40**:301 (Aug) 1939.

52 Bregman, A. Treatment of Erythema Multiforme Exsudativum with Sulfanilamide. Report of Case, *Arch Dermat & Syph* **38**:623 (Oct) 1938.

53 Eller, J. J. A Case for Diagnosis (Pemphigus? Dermatitis Herpetiformis?), *Arch Dermat & Syph* **37**:669 (April) 1938.

54 Caro, M. R. Pemphigus. Treatment with Sulfanilamide, Preliminary Report, *Arch Dermat & Syph* **37**:196 (Feb) 1938.

55 Lain, E. S., and Lamb, J. H. Treatment of Pemphigoid Eruption with Sulfanilamide. Report of Case, *Arch Dermat & Syph* **37**:840 (May) 1938.

A case of severe generalized impetigo herpetiformis in a pregnant woman was reported by Frank ⁵⁶ in which complete resolution occurred after sulfanilamide therapy. Improvement was noted on the third day after beginning treatment.

Several cases of various pyogenic dermatoses have been reported in which the condition was improved or cured by sulfanilamide. Abramowitz ⁵⁷ reported apparent cure in a case of sycosis vulgaris with moderate doses. The response was prompt. Strickler and Stone ⁵⁸ treated 4 patients with resistant sycosis vulgaris who responded within three weeks to sulfanilamide. The same authors reported 2 cases of impetigo neonatorum and 6 cases of secondary pyogenic dermatoses, in all of which the condition responded to this treatment. In the latter group of cases prolonged treatment was necessary.

Anderson and Halloran ⁵⁹ failed to obtain any improvement from sulfanilamide in a case of pyoderma gangraenosum.

Mercer ⁶⁰ successfully treated recurrent lymphangitis (elephantiasis nostras) of the lip which had resisted other forms of treatment.

Wright and Friedman ⁶¹ obtained decided improvement of a chronic streptococcic ulcer of the leg with sulfanilamide. These authors also used this drug in a case of infectious eczematoid dermatitis in which *Staphylococcus aureus haemolyticus* and *Streptococcus haemolyticus* were found. Complete healing took place in one week.

Thirty-one patients with erysipelas were treated by Iga and Kato ⁶² with small doses of sulfanilamide. All but 1 showed rapid and complete cure. One patient died, and 3 had recurrences which cleared up rapidly when treatment was resumed. Sulzberger ⁶³ has reported a case of recurrent erysipelas of the forehead and face which was successfully treated with sulfanilamide.

Sandler ⁶⁴ observed complete disappearance of all symptoms of syphilitic interstitial keratitis within ninety-six hours after sulfanilamide therapy had been instituted.

56 Frank, L. J. Impetigo Herpetiformis. Report of Successful Treatment with Sulfanilamide, *Arch Dermat & Syph* 40 253 (Aug) 1939

57 Abramowitz, E. W. Sycosis Vulgaris, Improved by Sulfanilamide, *Arch Dermat & Syph* 37 1086 (June) 1938

58 Strickler, A., and Stone, M. J. Sulfanilamide in Treatment of Pyogenic Dermatoses, *Arch Dermat & Syph* 40 244 (Aug) 1939

59 Anderson, C. R., and Halloran, D. R. Pyoderma Gangraenosum, *Arch Dermat & Syph* 39 361 (Feb) 1939

60 Mercer, S. R. Recurrent Lymphangitis Treated with Sulfanilamide, *Arch Dermat & Syph* 39 1042 (June) 1939

61 Wright, C. S., and Friedman, R. Chronic Streptococcic Ulcer of the Skin Responding to Sulfanilamide, *Arch Dermat & Syph* 39 554 (March) 1939

62 Iga, Y., and Kato, T. *Acta dermat* 30 112, 1937

63 Sulzberger, M. B. Recurrent Erysipelas Successfully Treated with Sulfanilamide, *Arch Dermat & Syph* 40 498 (Sept) 1939

64 Sandler, I. L. Sulfanilamide Treatment of Syphilitic Interstitial Keratitis, *Arch Dermat & Syph* 39 528 (March) 1939

In the treatment of lymphogranuloma venereum sulfanilamide has apparently been consistently beneficial Shaffer and Arnold⁶⁵ treated 46 patients, in all of whom there was definite improvement Of 22 patients on whom continued observation was possible, 4 were completely cured, 11 were decidedly improved and 4 failed to return, there were 3 failures Montel and Nguyen-van-Tho⁶⁶ reported 3 cases in which complete recovery occurred Warren⁶⁷ reported approximately 20 per cent improvement from sulfanilamide in a case in which the condition had resisted all treatment for three years Greenbaum⁶⁸ obtained definite improvement in 3 cases in which the eruption had been unaffected by other treatment

The reports on the treatment of chancroid with sulfanilamide have been almost universally favorable Kornblith, Jacoby and Wishengrad⁶⁹ reported 45 cases of proved chancroid in which cure was obtained without failure by the end of the second week Eighty grains (5.2 Gm) of sulfanilamide was given daily for five days and then 40 grains (2.6 Gm) daily for nine days Fox⁷⁰ treated a patient with an extensive chancroidal ulcer of the penis and obtained complete cure in twenty-eight days He also reported a case in which a total of 52 Gm of sulfanilamide was administered without apparent improvement Lepinay⁷¹ stated that the use of sulfanilamide as a dusting powder was extremely effective against chancroid For early lesions he used the drug only locally, but for conditions in the late stages he gave the drug both locally and internally Healing in his cases was rapid, the time necessary for cure being generally one week or less In 2 cases reported by Schwartz⁷² cure of the ulcer and of the ruptured bubos was obtained within two weeks Chargin⁷³ reported cure within two weeks of a long-standing chancroidal infection Rostenberg⁷⁴ obtained

65 Shaffer, L. W., and Arnold, E. Lymphogranuloma Venereum, Especially Its Treatment with Sulfanilamide, *Arch Dermat & Syph* 38:705 (Nov) 1938

66 Montel, L. R., and Nguyen-van-Tho. *Bull Soc franç de dermat et syph* 45:652, 1938

67 Warren, L. H. Lymphogranuloma Venereum, *Arch Dermat & Syph* 38:262 (Aug) 1938

68 Greenbaum, S. S., in discussion on Warren⁶⁷

69 Kornblith, B. A., Jacoby, A., and Wishengrad, M. Treatment of Chancroid with Sulfanilamide, *J A M A* 111:523 (Aug 6) 1938

70 Fox, H. Chancroidal Ulcer of Long Standing Cured by Sulfanilamide, *Arch Dermat & Syph* 38:660 (Oct) 1938

71 Lepinay. *Bull Soc franç de dermat et syph* 45:1728, 1938

72 Schwartz, W. F. Chancroid with Ruptured Bubo Treated with Sulfanilamide, *Arch Dermat & Syph* 40:331 (Aug) 1939

73 Chargin, L. Chancroid, Cured with Sulfanilamide. Lymphogranuloma Venereum, Syphilis, *Arch Dermat & Syph* 38:476 (Sept) 1938

74 Rostenberg, A. Chancroids Cured with Sulfanilamide, *Arch Dermat & Syph* 38:509 (Sept) 1938

cure within two weeks in a case of chancroid in which other methods had been used for four months

PERSONAL EXPERIENCE WITH SULFANILAMIDE

Of 19 patients with erysipelas treated with sulfanilamide, 16 were either rapidly cured or greatly improved and disappeared from observation. Three patients died within twenty-four hours after treatment was instituted, 1 was a man aged 93, and the conditions in the other 2 were severe and unusually extensive when treatment with sulfanilamide was begun. In general this experience coincides with that reported in the literature.

Of 9 patients with erythema multiforme treated with sulfanilamide, in 1 the condition occurred as a dermatophytid associated with an acute dermatophytosis of the feet, the injection of trichophytin intracutaneously produced an iris type lesion similar to those of the disease. There was no improvement from the sulfanilamide. All the other patients responded in from two to five days, and in all remarkable improvement was noted within twenty-four hours. In a patient who was somewhat intolerant to the drug there was a recurrence of the condition, but it disappeared permanently after further administration of the drug.

Three patients with impetigo contagiosa were cured in five, five and nine days, respectively, without the use of local germicidal preparations.

Although a majority of the reports indicate decided benefit from sulfanilamide therapy in patients with lupus erythematosus, my experience has not been so favorable. Only 1 patient was cured by it. Of 5 with discoid conditions, 2 were slightly improved and the others were apparently unaffected. Four patients with acute disseminated lupus erythematosus were benefited to varying extents, but only 1 was cured, this patient, however, was healed in about ten days. One patient obtained moderate improvement for a time and then died after abortion and lobar pneumonia. Sulfanilamide is by no means consistently beneficial in the treatment of lupus erythematosus. Some patients are greatly benefited, and others are uninfluenced by the drug.

Four patients with chronic lymphangitis of streptococcic origin were treated. One of these had been having periodic exacerbations with chills and fever every month or six weeks. After three weeks of sulfanilamide therapy he was well and has had no recurrence for the past year. Two other patients were cured, and 1 was considerably benefited.

A woman with streptococcic stomatitis and cheilitis was definitely improved after twenty-four hours of sulfanilamide treatment. She then disappeared from observation, but I learned later that the condition had cleared up rapidly.

Of 2 patients with typical pemphigus treated with sulfanilamide, neither was apparently influenced.

A patient with an acute bullous eruption which closely resembled pemphigus but with a negative Nikolsky sign showed rapid improvement and was cured in approximately three days. This condition probably belongs to the erythema multiforme group.

A patient with dermatitis herpetiformis received no benefit from sulfanilamide given over two weeks.

Two patients treated for chancroid showed definite and prompt improvement. One disappeared from observation after the first few days of treatment, and further observation was not possible. The other experienced such an unfavorable reaction to the drug that its administration was discontinued at the end of the fourth day, at which time there was about 50 per cent diminution in the size of the ulcer.

A patient with lymphogranuloma venereum was treated with sulfanilamide. The condition was a recurrence of an old infection which had been inactive for approximately four years. After ten days' treatment there was definite improvement, and the patient was not seen again.

A patient with moderately severe herpes zoster accompanied by considerable pain was treated for three days with sulfanilamide. There was no change in the physical signs or in the intensity of the pain.

A patient with recurring furunculosis was treated for one week, without showing evidence of any improvement.

SUMMARY

The history of sulfanilamide therapy is presented, together with its mode of action and toxic manifestations. A review of the literature concerning the treatment of dermatologic conditions and a discussion of my experience are given for the purpose of evaluating sulfanilamide therapy in dermatology.

Apparently the drug is of definite value in the majority of cases of the following conditions: erysipelas, erythema multiforme, impetigo contagiosa, acute disseminate lupus erythematosus, chancroid and streptococcic lymphangitis.

Sulfanilamide appears to be of value in some cases of the following diseases and worthy of further testing: chronic lupus erythematosus, lymphogranuloma venereum, sycosis vulgaris and pemphigus.

IODOBISMITOL WITH SALIGENIN IN THE TREATMENT OF NEUROSYPHILIS

GEORGE V KULCHAR, M D

CHARLES W BARNETT, M D

AND

JOHN F CARD, M D

SAN FRANCISCO

After many years of experimental search for a preparation which would produce a significant concentration of bismuth in the central nervous system, Hanzlik, Mehrtens, Gurchot and Johnson¹ introduced iodobismitol (sodium iodobismuthite dissolved in ethylene glycol containing 12 per cent sodium iodide) in 1930. The administration of this preparation to animals resulted in greater amounts of bismuth in the nervous system than were obtained with other available compounds. These findings suggested that iodobismitol might be of exceptional value in the treatment of neurosyphilis, and this theoretic effectiveness was supported by the preliminary clinical studies of Mehrtens and Pouppirt.² No further clinical evaluation of this preparation in the treatment of neurosyphilis has been made, although Johnson and Barnett³ have shown that its use in the routine treatment of early syphilis does not prevent involvement of the nervous system.

Thorough investigation in the laboratory is essential before any drug may be used clinically, but no matter how complete this investigation, it can only suggest the possible therapeutic value. The final evaluation must depend on extensive clinical trial. In cases of neurosyphilis the problem is particularly difficult, because improvement with treatment is at best slow and uncertain. Moreover, comparable controls are not available, since it is not feasible to allow patients to go untreated because of the gravity of neurosyphilis.

From the Department of Medicine, Stanford University School of Medicine

1 Hanzlik, P J, Mehrtens, H G, Gurchot, C, and Johnson, C C. Iodobismitol, a Soluble Bismuth Product for Use in the Treatment of Syphilis. Preliminary Report, J A M A 98 537 (Feb 13) 1932

2 Mehrtens, H G, and Pouppirt, P S. Iodobismitol in the Treatment for Neurosyphilis, Arch Neurol & Psychiat 26 1220 (Dec) 1931

3 Johnson, G S, and Barnett, C W. The Effect of Iodobismitol upon Spinal Fluid Findings in Early Syphilis, Am J Syph, Gonorr & Ven Dis 20 651 (Nov) 1936

The results obtained with iodobismutol with saligenin N N R (a solution of sodium iodobismuthite and sodium iodide in propylene glycol containing saligenin and a small amount of acetic acid) in the treatment of syphilis have been previously reported,⁴ but no detailed consideration was given to neurosyphilis. The present study is concerned with the effect of treatment in 203 patients with various types of syphilis of the central nervous system. All had received iodobismutol with saligenin and had been under observation for at least six months, and patients who had been given either intraspinal or fever therapy were excluded.

Of the 203 patients, 129 were male, and 74, female. The ages ranged from 13 to 66, with an average of 44 for the males and 39 for the females. The initial diagnosis was tabes dorsalis in 68 patients, dementia paralytica in 44, dementia paralytica with tabes dorsalis in 18, meningo-vascular neurosyphilis in 22 and asymptomatic neurosyphilis in 51.

Prior to treatment detailed histories were taken, and complete physical and neurologic examinations were made, and these were repeated at approximately six month intervals. At least two examinations of the cerebrospinal fluid were made in all but 12 patients, the total number of examinations being seven hundred and three, or an average of three and a half per patient. The duration of treatment averaged thirty-three months, and the total period of observation, thirty-five months. Many patients were still under treatment at the time this study was terminated.

The method of classification of abnormalities of the spinal fluid was that used by the Cooperative Clinical Group. Group II fluids have a normal or increased cell count, protein content and colloidal gold curve and a positive Wassermann reaction. Group III consists of fluids of the dementia paralytica type. There were no fluids initially in group I. Quantitative Wassermann reactions were used in the evaluation of results, and whenever there was a decrease in titer under treatment, the fluid was considered to be improved. A decided fall in cell count or in protein content, as measured by qualitative globulin tests and the colloidal gold curve, was also classified as improvement, even though in some instances the Wassermann titer did not change. When only minor changes occurred in any of the reactions, the fluid was considered unchanged, but if any increase in the degree of positivity was noted, the condition was regarded as worse. All fluids that became normal were classified as showing reversal of reaction rather than as improved.

The clinical results have been evaluated according to the following terms. (1) much improved, if the symptoms practically disappeared and the progress of the disease was arrested; (2) moderately improved,

⁴ Barnett, C. W., and Kulchar, G. V. Iodobismutol in the Treatment of Syphilis, *J. A. M. A.* 109:1715 (Nov 20) 1937.

when the symptoms became less severe, (3) unchanged, if symptoms and signs were not significantly altered, and (4) worse, if there was definite progression. Because of the relatively small number of cases it was found inadvisable to consider separate diagnoses. Consequently the series was left undivided in the final compilation of the data.

Although all patients received iodobismutol with saligenin, many also had other forms of chemotherapy. In this report the therapy was of three types: (1) iodobismutol with saligenin exclusively in intramuscular doses of 2 or 3 cc. one to three times weekly, (2) neoarsphenamine in addition to iodobismutol with saligenin (there was a considerable variation in the amount of neoarsphenamine used, but no patients who received less than a total of 5 Gm. were included) and (3) tryparsamide with or without neoarsphenamine in addition to iodobismutol with

TABLE 1—*The Results of Treatment with Iodobismutol with Saligenin for One Year in Patients with Neurosyphilis, Compared with Those Obtained by Mehrtens and Pouppirt*

	Mehrtens and Pouppirt Per Cent	Present Series Per Cent
Cerebrospinal fluid response		
Reversed	7	10
Improved	12	43
Unimproved	51	43
Clinical response		
Improved	61	61
Unimproved	36	39
Wassermann response		
Reversed	15	25
Improved	25	37
Unimproved	60	34

saligenin (there was again a variation in the amount of tryparsamide, but patients who had less than 30 Gm. were excluded).

Iodobismutol with saligenin has been used in this clinic almost to the exclusion of other heavy metal preparations during the last ten years. We are consequently unable to compare its effectiveness with that of other bismuth preparations used under similar conditions. The evaluation must, therefore, be based on the relative effects of varying amounts of iodobismutol with saligenin, both with and without other forms of chemotherapy. We have accordingly tabulated the data to determine the serologic and clinical results of the three types of therapy outlined above.

In the initial report of Mehrtens and Pouppirt the clinical and serologic results of treatment with iodobismutol alone for one year are given. In the present series there is a similar group of 54 patients who received iodobismutol with saligenin exclusively for one year. A comparison of the results of this form of treatment in these two groups of patients is made in table 1.

The results in the two groups are strikingly similar and suggest that the bismuth compound has a definite therapeutic effect in cases of neurosyphilis. Both the clinical and the serologic results appear exceptionally good for this period of time. This might be interpreted as evidence of a high degree of therapeutic efficacy, but it must be kept in mind that both series comprised ambulatory patients among whom there was a low incidence of advanced neurosyphilis. In cases of this type a rapid response is much more common than in the more advanced stages. If the excellent results are due to the effectiveness of iodobismutol, one might expect that the degree of improvement would vary according to

TABLE 2—*Comparison of Serologic and Clinical Results in Patients Receiving Less Than and More Than 12 Gm of Iodobismutol with Saligenin in One Year*

Total Dose of Iodobismutol with Saligenin	Cerebrospinal Fluid Response		Clinical Response	
	Number of Patients	Per Cent Improved	Number of Patients	Per Cent Improved
More than 12 Gm	23	57	19	63
Less than 12 Gm	26	54	20	60

TABLE 3—*Comparison of Cerebrospinal Fluid and Clinical Response in Patients Treated for Various Periods with Iodobismutol with Saligenin Exclusively*

Duration of Treatment	Cerebrospinal Fluid Response		Clinical Response	
	Number of Patients	Per Cent Improved	Number of Patients	Per Cent Improved
Six months	18	50	16	63
One year	49	55	41	61
Two years	25	64	21	62

the amount of iodobismutol administered. To test this assumption the patients treated with iodobismutol with saligenin alone for one year have been divided into two approximately equal groups according to the amount received. The clinical and serologic results in patients receiving more than 12 Gm (approximately one hundred injections) during one year are compared with those in patients receiving less than 12 Gm in table 2.

From the data in table 2 it appears that there is no correlation between the response and the amount of iodobismutol with saligenin received during one year. However, many of the patients, even though included in the second group, received large amounts of iodobismutol with saligenin. All attempts to segregate groups receiving small amounts of the bismuth preparation led to the inclusion of patients who had great irregularity of treatment, when the period of observation was kept at one year. We have accordingly compared the results obtained

in patients treated with iodobismutol with saligenin alone for periods of six months, one year and two years. The results are shown in table 3.

From table 3 it is evident that the improvement is not proportional to the amount of iodobismutol with saligenin received. Although there is a slight increase in the number of cerebrospinal fluids improved, there is no relation between duration of treatment and the clinical results. The improvement after six months of treatment is greater than can be expected from the natural involution of the disease. It appears that iodobismutol with saligenin has definite therapeutic value, but the maximum effect is achieved during the first few months of treatment.

In order to compare the effect of iodobismutol with saligenin alone with that of iodobismutol with saligenin plus other forms of chemo-

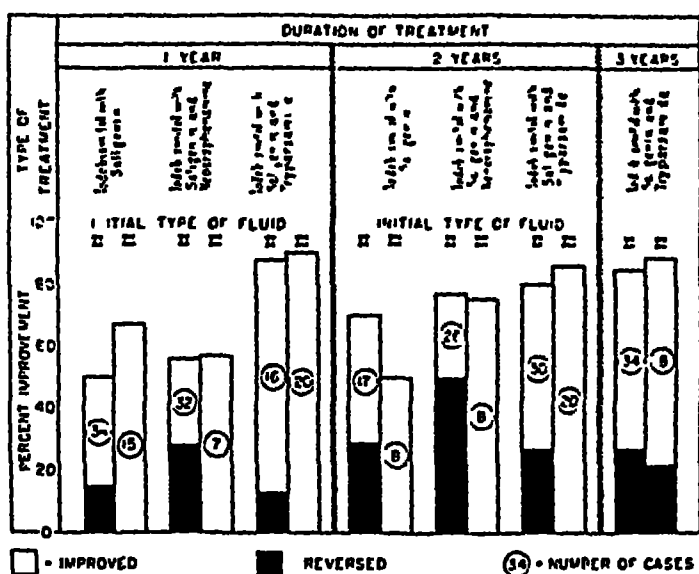


Fig 1—Cerebrospinal fluid response to iodobismutol with saligenin alone and in combination with neoarsphenamine or tryparsamide

therapy, the results of treatment were evaluated at periods of approximately one year and two years. The serologic results, based on the initial type of spinal fluid, are shown in figure 1.

At the end of the first year about one half of the type II spinal fluids were improved with treatment with iodobismutol with saligenin alone. When neoarsphenamine was combined with iodobismutol with saligenin, the percentage of improvement was slightly greater and that of reversal of reaction almost doubled. With the addition of tryparsamide therapy, the incidence of serologic improvement was greatly increased. The percentage of reversal was, however, less than that obtained with other forms of treatment. This probably is due to the fact that tryparsamide therapy was often reserved for patients whose cerebrospinal fluids were refractory to other forms of treatment. In

none of the type III fluids was the reaction reversed, but the greatest improvement occurred in patients who received tryparsamide. Although the patients receiving neoarsphenamine showed a slightly lower incidence of improvement, the number is too small to be of significance.

At the end of the second year the serologic results were similar to those obtained during the first year. The percentage of improvement was generally increased, and the proportion of reversals of reaction was considerably greater. As seen in the results of the first year, the addition of either neoarsphenamine or tryparsamide to iodobismutol with saligenin improved the results. While the total incidence of improvement with tryparsamide at the end of two years is not greater, there is a definite increase in the percentage of reversals of reaction. None

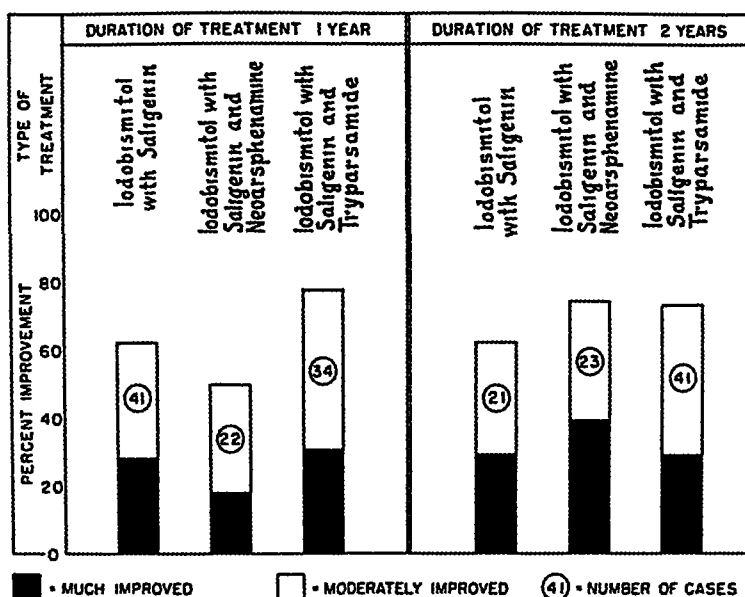


Fig 2—Clinical results of treatment with iodobismutol with saligenin alone and in combination with neoarsphenamine or tryparsamide (results in patients with asymptomatic neurosyphilis are not included)

of the type III spinal fluids showed a reversal of reaction during either the first or second years with any of the three methods of treatment. The results of tryparsamide therapy at the end of the third year are included in figure 1, showing an increase in the degree of improvement, despite the fact that there is no change in the percentage of the fluids improved. Data are not available for the results of either iodobismutol with saligenin alone or in combination with neoarsphenamine for the three year period, as practically all patients treated for more than two years received tryparsamide.

The clinical improvement obtained with the three types of therapy at the end of one year and two years is shown in figure 2.

There is striking similarity between figures 1 and 2, indicating that in general clinical and serologic improvement parallel each other. In the unimproved group a few patients are included who became clinically worse during treatment, but these were too scattered to be of significance and have been disregarded. After one year the percentage of clinical improvement with iodobismutol with saligenin alone is greater than that secured with the addition of neoarsphenamine but considerably less than that obtained with the addition of tryparsamide. At the end of two years, however, the improvement secured with iodobismutol with saligenin and either neoarsphenamine or tryparsamide is greater than with the bismuth compound alone. When iodobismutol with saligenin is used alone or in combination with tryparsamide, the clinical improvement, both in amount and in degree, is practically the same after one year and after two years of treatment. This indicates that when improvement occurs with these two types of therapy, it does so promptly and is then sustained. With the addition of neoarsphenamine this is not true, since definite improvement continues during the second year.

SUMMARY

The clinical and serologic results obtained in 203 patients with various types of neurosyphilis after treatment with iodobismutol with saligenin alone and in combination with neoarsphenamine or tryparsamide are reported.

The therapeutic effect of iodobismutol with saligenin in patients with neurosyphilis is achieved rapidly and is not increased by prolonged administration. The effect, however, is definitely enhanced by the addition of either neoarsphenamine or tryparsamide, particularly the latter. Iodobismutol with saligenin is of value in the treatment of neurosyphilis, but it should not be used ordinarily as the only form of therapy.

EXFOLIATIVE DERMATITIS DUE TO NAPHTHALENE

REPORT OF AN ERUPTION RESEMBLING MYCOSIS FUNGOIDES

S J FANBURG, M D

NEWARK, N J

There is a group of patients, frequently encountered by dermatologists, who have a dermatosis of a protean nature during the evolution of which there is always a phase which resembles mycosis fungoides or dermatitis herpetiformis. The eruption is further characterized by a tendency to clear up rapidly, especially during hospitalization, only to recur with equal rapidity when the patient returns to his usual environment. Sulzberger and Garbe¹ have collected and reported 9 cases of such a condition under the title "Distinctive Exudative Discoid and Lichenoid Chronic Dermatoses." Cannon² collected and reported 8 cases under the title "Allergic Dermatitis Simulating Lymphoblastoma." While an allergic basis for the conditions in these cases was surmised by Cannon from the clinical course, Sulzberger and Garbe could not find sufficient evidence to "consider this dermatosis as a representative form of any known atopic manifestation, although it may be some form of sensitization dermatosis."

I have observed a patient whose dermatosis fulfilled all the requirements of the condition described by these authors but in whose case I was able to find an allergen, naphthalene, the elimination of which was responsible for the disappearance of the process. The dermatosis resembled mycosis fungoides so closely that several competent dermatologists made that diagnosis clinically, and their impressions were strengthened by independent histologic reports on different pieces of tissue by Drs. Walter Highman and Fred D. Weidman suggesting that diagnosis. The elimination of naphthalene, ordinarily used in households as moth balls or flakes, from the patient's environment resulted in prompt recovery, which has lasted uninterruptedly for seven years.

REPORT OF A CASE

History—X. Y., a physician aged 43, born in Russia, was in good health until October 1930. After a severe nervous strain due to the illness of his wife, some

1 Sulzberger, M. B., and Garbe, W. Nine Cases of Distinctive Exudative Discoid and Lichenoid Chronic Dermatoses, *Arch. Dermat. & Syph.* **36**:247 (Aug.) 1937.

2 Cannon, A. B. Allergic Dermatitis Simulating Lymphoblastoma, *Arch. Dermat. & Syph.* **39**:846 (May) 1939.

pruritic papules developed on the dorsal surfaces of his fingers and hands. They were rapidly followed by a generalized, profuse erythematous-squamous eruption. There was severe itching accompanied by a burning sensation. Perspiration was profuse, especially at night. The slightest effort induced physical exhaustion, and the patient became irritable and apprehensive. His insomnia was persistent and yielded but slightly to sedatives. About six weeks after the onset of the eruption he entered a midwestern private sanatorium. Improvement began almost immediately after an operation for hemorrhoids. In the third week of his stay at the institution he suffered a mild relapse, consisting of itching, erythema and slight scaling. This attack was attributed to the eating of asparagus and to an unbalanced nervous mechanism. At the end of the fourth week he came home greatly improved. After the first night at home a progressive generalized eruption developed, for which he entered the Beth Israel Hospital in New York. Improvement began within twenty-four hours, and after three weeks he was sufficiently well to leave the hospital. Instead of returning home he went to stay with a relative in a nearby town. Within a day the itching, perspiration and scaling returned. On March 13, 1931 he entered the Newark Beth Israel Hospital, and again within a few days the acute symptoms subsided. He remained in the hospital five weeks. About two days after his return home exfoliation began again.

On April 25, through the kindness of Dr. Howard Fox, I saw this man for the first time and had him hospitalized in Mount Sinai Hospital in New York. The acute phase of the attack subsided in twenty-four hours. He was confined in this hospital for eight weeks. He then spent six weeks in the mountains of New York, where his recovery persisted. Two days after his return home he had an acute exacerbation. He was readmitted to the Newark Beth Israel Hospital in September, and his condition improved quickly. He stayed in the hospital nineteen weeks, after which he went to the seashore. His condition was unchanged for three days, but on the fourth day he sustained an acute exacerbation coincident with the receipt of a trunkful of clothes from his home. He stayed on at the seashore and became progressively worse. In February 1932 he returned to the Newark Beth Israel Hospital. At that time his cutaneous condition was worse than it had ever been. However, improvement began immediately after admission and was continuous for two weeks, when a mild relapse lasting a few days occurred. This relapse followed contact with a pair of white duck trousers which were brought from home for the patient to wear in the hospital. A few hours after he put them on itching became intense, and new urticarial lesions appeared. Careful inquiry revealed that the trousers had lain several months in a drawer with naphthalene moth flakes. Contact tests with naphthalene gave, within ten hours, an erythematous reaction accompanied by generalized pruritus and crops of urticarial lesions. This test was repeated on several occasions with similar results. The results of contact tests with numerous other substances were negative. The patient was discharged from the hospital May 25. For the past seven years there have been no relapses, and with the exception of the appearance of a few transitory itchy papules, his skin has been normal. He returned to his home and is actively engaged in his profession, but he carefully avoids naphthalene.

Clinical Examination—In April 1931, when I first saw this man, he presented a generalized erythematous eruption with exfoliation in large flakes. The palms, soles and mucous membranes were exempt. There were also a few scattered areas free from eruption on the chest and back. On the face, neck, chest, back and dorsal surfaces of the hands were brownish red infiltrated nodules, 5 to 30 mm in size. There was generalized enlargement of the lymph nodes, especially noticeable

in the inguinal regions. The chest was emphysematous, with the heart enlarged to the right, and the liver was palpable about 2 fingerbreadths below the costal margin. The blood pressure was 110 systolic and 76 diastolic.

Laboratory Examinations—Numerous examinations of the blood showed eosinophils ranging from 10 to 38 per cent. There was usually leukocytosis, but the erythrocytes and hemoglobin were within normal limits. The chemical examination of the blood gave normal results. Examination of the stools showed no parasites. Contact or patch tests with numerous substances obtained from his home all gave negative results with one outstanding exception, naphthalene moth flakes.

Roentgen ray examinations of the lungs showed moderate emphysema and thickened pleura of the right lung, it was also noted that the heart was enlarged to the right and that the aorta was sclerotic and moderately dilated. Roentgenograms of the teeth showed no apical infiltrations, those of the gastrointestinal tract revealed appendicular stasis lasting beyond the fourth day. The gallbladder was not definitely visualized, and examination of the bile gave essentially negative results. No arsenic was found in the urine.

Histologic Examination—Dr. Fred D. Weidman on March 4, 1932, wrote as follows:

"The changes shown in the section are compatible with those of granuloma fungoides, and I can understand how the lesion could be that of mycosis fungoides, as it is understood at present dermatologically. By that I mean that there is a large group of cutaneous vices which will probably some day be shown to have the capacity of inducing the anatomic changes of that disease. I know of at least 1 case in which the cutaneous mycosis fungoides turned out to be Hodgkin's disease at necropsy, and it is probable that other vices of the reticuloendothelial system also have the power to produce dermatologic mycosis fungoides.

"The histologic features which are of value in corroborating Dr. Schamberg's diagnosis consist in, first, the high grade hyperplasia and edema of the epidermis, resulting in such a uniform swelling of epidermal pegs that their normal distribution and relations are scarcely disturbed. Secondly, the round cell infiltration of the corium is of sufficient grade to qualify as granuloma fungoides.

"There are two shortcomings for a diagnosis of granuloma fungoides, first, the absence of round cell infiltration of the epidermis (so-called abscesses of Pautrier), which is not so important, and, secondly, the comparative uniformity of the round cell types concerned in the infiltration. Thus, whereas there are moderate numbers of eosinophils present, the remaining cells are almost exclusively of a plasma cell type. This makes me wonder whether they might be myelocytes or perhaps cells of myeloma. Incidentally, the establishment of either of these conditions in a patient would not vitiate the sense of granuloma fungoides dermatologically but only amplify and substantiate suspicions that have been entertained a long time."

Dr. Walter Highman examined a different biopsy specimen made a year later and rendered the following report:

"With eosin and hematoxylin stain and low power magnification, the epidermis is surrounded by a moderately thick continuous scale, presenting numerous islands of parakeratosis. Below this there is a moderately thickened but not continuous granular layer, in places consisting of six or eight rows of cells. The entire system of rete pegs is almost uniformly three or four times its normal depth, with some of the pegs narrow and tongue-like and others fused together in groups of four or five, uniformly or enclosing areas of islands or tips of the papillae. The papillary

body is correspondingly changed in contour and presents a definite but not dense infiltration. The entire level of the subpapillary plexus presents a similar infiltration, which consists of dense foci, prevailing circular or oval, lying in the background of sparse infiltration and edematous collagen. The area involved is the upper half of the cutis. The subcutaneous tissue is virtually without abnormalities.

"With high power it is seen that the cells of the suprapapillary rete are separated from one another by slightly exaggerated intercellular spaces showing stretched epithelial threads. This change becomes more marked in the pegs and is most definite nearest the basal layer. The basal membrane is intact. Nevertheless, throughout the pegs wandering cells are found, which apparently have migrated and which are chiefly from the tips of the papillae. A great many mitotic figures are seen in the pegs. The papillae present great numbers of dilated capillaries engorged with red blood cells. Around these capillaries are seen fibroblasts, lymphocytes and eosinophils in fairly even mixture and plasma cells, from 4 to 10 per field. The infiltration at the subpapillary level looks like that in the papillae, where it is diffuse, except that there is a greater number of plasma cells. The denser or focal areas appear clustered in dilated lymphatic spaces, are richer in fibroblasts and plasma cells and present a constant but not great number to the field of a large cell. This cell has a body somewhat irregular in outline and tends to have one or more angles, sometimes even one or two fine prolongations of the cytoplasm. A not great but definite amount of cellular detritus is seen. Here and there are large cells with two nuclei, which appear to be something more than merely fused round cells. A certain number of dividing cells are seen.

"The picture is one of a chronic scaling dermatitis, with a sluggish infiltration, highly variegated in its cellular elements and suggestive of activity in the lymphatic system, such as is seen in mycosis, although no positive opinion that this condition is mycosis can be expressed. A slide from the Mount Sinai Hospital dating from an earlier period is similar in composition."

Clinical Course and Treatment—As has been stated in the history, the clinical course was characterized by periods of exacerbation and remission. One is struck by the fact that the exacerbations usually followed the patient's return home, and the acute symptoms always subsided quickly on admission to hospital. Many plans of treatment were carried out. Among these were injections of sodium thiosulfate, splenic extract, calcium gluconate and strontium bromide and the use of autohemotherapy, superficial roentgen therapy, restricted diets, colonic irrigations, baths, powders and bland ointments. During remissions the skin did not entirely return to normal. The exfoliation disappeared, and the skin became soft and pliable, but crops of urticarial lesions continued to appear, especially about the abdomen and neck. Some of these lesions were persistent, lasting for months. This was particularly true of those on the abdomen and on the backs of the fingers. Itching became less marked but interfered with sleep at night. The appetite was usually good. It was thought for a long time that the acute exacerbations on the patient's return home could be explained by an intense psychic strain produced by nervous tension, but there was little to support this theory.

The earliest case that I could find recorded in which naphthalene affected the skin was reported by Evers³ in 1884. In this case there were nausea, abdominal pains, anorexia, insomnia, sweating and pruritus.

3 Evers. *Erkrankung, anscheinend herforgerufen durch Naphthalin*, *Berlin Wehnschr* 21 593 (Sept 15) 1884.

The condition resulted from naphthalene dusted on furniture. Several cases of poisoning from naphthalene are reported in children who had eaten moth balls ⁴. Symptoms were those pointing to involvement of the nervous system, such as staggering gait, mental dulness, burning sensation in the urethra, nausea and vomiting. Ocular lesions have been produced in rabbits ⁵ and in human beings ⁶ by the administration of naphthalene. Recently Touraine and Ménétrel ⁷ described several cases of various dermatoses in workers exposed to hot naphthalene and to its chlorine derivatives. The chloronaphthalenes are used chiefly as waterproofing agents and may produce acne in workers exposed to their fumes.

Naphthalene is a product of the distillation of coal tar. The tar contains about 6 per cent of it. It is a hydrocarbon of the formula $C_{10}H_8$, known also as tar camphor, white tar or naphthalin. It occurs as white crystalline flakes or powder and has a strong coal tar odor. It melts at 80 C and boils at 217.9 C. It is moderately volatile at ordinary temperature. It is insoluble in water but soluble in absolute alcohol, ether and benzene. It is used chiefly in the manufacture of dyes and as a moth repellent in households.

COMMENT

The ultimate result in this case, if the precipitating cause of the eruption had not been determined, cannot be foreseen, but it is interesting to speculate. The damage to the patient's reticuloendothelial system could have been carried to such an extent that true mycosis fungoides, or possibly Hodgkin's disease, might have developed, owing to repeated insults to that system. I purposely refrained from reporting this case at an earlier date, because I was so impressed with the clinical diagnosis of granuloma fungoides that the positive reactions to naphthalene were not too convincing at the time. Seven years has elapsed without any recurrence, and I feel that mycosis fungoides can

4 Peterson, F., Haines, W. S., and Webster, R. W. *Legal Medicine and Toxicology*, Philadelphia, W. B. Saunders Company, 1923. Zangerle. *Therap. Monatsh.* **13**:122, 1899, cited by Peterson, Haines and Webster, p. 694. Nash, L. F. Naphthalene Poisoning, *Brit. M. J.* **1**:251, 1903, cited by Peterson, Haines and Webster, p. 694.

5 Michail, D., and Vancea, P. Sur la multiplicité des voies par lesquelles on peut produire des lésions oculaires naphthaliniques, *Compt. rend. Soc. de biol.* **96**:63-65, 1927.

6 Lewin, L., and Guillery, H. Die Wirkungen von Arzneimitteln und Giften auf das Auge. *Handbuch für die gesamte ärztliche Praxis*, Berlin, A. Hirschwald, 1905, vol. 1, p. 696.

7 Touraine, A., and Ménétrel, B. Dermatoses professionnelles par la naphthalène et ses dérivés, *Prat. méd. franç.* **15**:335-346 (May, B) 1934.

be definitely excluded. The prompt and lasting recovery on elimination of naphthalene from the patient's environment points definitely to that agent as the causative factor in this case.

SUMMARY

Previous writers have described dermatoses resembling lymphoblastomas, which they surmised were of allergic origin. My case of naphthalene dermatitis resembling mycosis fungoides clinically and histologically suggests that the connecting link between surmise and fact has been established.

This case suggests that more careful allergic study be made in proved as well as suggestive cases of lymphoblastomas, especially those with a history of remissions while the patient was hospitalized.

PEMPHIGOID ERUPTION ASSOCIATED WITH HEMORRHAGIC NEPHRITIS FOLLOWING BISMUTH THERAPY

REPORT OF A CASE

BERTRAM SHAFFER, M D

AND

LEON H COLLINS JR, M D

PHILADELPHIA

The constant introduction of new bismuth compounds¹ into syphilotherapy makes it necessary to call attention to dangerous complications from well established forms of bismuth medication, in order that physicians may not lose sight of these unusual but grave potentialities. We have had the opportunity of studying a patient with a generalized bullous eruption and hemorrhagic nephritis following the use of bismuth, which because of the rarity of these manifestations was deemed worthy of reporting.

Muller,² Boas³ and Langer⁴ mentioned that "bullous exanthems" may occur after the administration of bismuth, but they gave no details and apparently no references to reports of cases. Juliusberg⁵ mentioned that Muller has reported a bullous eruption of the type of dermatitis herpetiformis, but in the references which were available to us we were unable to find such a report. The only reference⁶ which we could not obtain might well have contained the description of this case.

From the Department of Dermatology and Syphilology, John H Stokes, M D., Director, and the Department of Medicine, O H Perry Pepper, M D., Director, Hospital of the University of Pennsylvania

1 (a) Meininger, W M, and Barnett, C W. The Treatment of Syphilis with Sobisminol Mass Given by Mouth, J A M A **113**:2214-2218 (Dec 16) 1939 (b) Scholtz, J R, McEachern, K D, and Wood, C. Sobisminol Mass Clinical Results with Oral Administration, *ibid* **113**:2219-2223 (Dec 16) 1939

2 Muller, H. Wismutbehandlung der Syphilis, Zentralbl f Haut- u Geschlechtskr **7**:289-300, 1922

3 Boas, K. Ueber toxische Hauterscheinungen im Verlaufe der Wismutbehandlung der Syphilis, Med Klin **20**:1571-1573, 1924

4 Langer, E. Die Nebenerscheinungen bei der Wismutbehandlung der Syphilis, Klin Wchnschr **7**:554-559, 1928

5 Juliusberg, F. Die Nebenwirkungen der Wismutbehandlung, in Jadassohn, J. Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol 18, pp 465-466

6 Müller, H. Weitere Versuche der Syphilisbehandlung mit Wismut, Munchen med Wchnschr **69**:1659, 1922

We could find no mention of eruptions of this type in either the French or the English literature. The nearest approach to such a condition was in a report by Catzeffis⁷ who described a patient with a bullous eruption of the forearms and hands in association with severe pain, redness and swelling of the involved parts and erythema of the abdomen.

Hemorrhagic nephritis in contrast to toxic nephrosis, is similarly a most unusual complication of bismuth medication. Many investigators, among whom are Fournier⁸, Gaté⁹, Dowds¹⁰, Schröder¹¹, Leff¹² and Galliot¹³ who discussed the nephritic effects of this drug did not even mention this type of reaction. Others, i. e. Bory¹⁴ and Eitzen¹⁵ stated that at times a few red cells may appear in the urine in connection with a bismuth toxic nephrosis.

On the other hand Galliot¹⁶ reported a fatal case of hemorrhagic nephritis in association with purpura, while Gawalowski¹⁷ and Dassen and Rey¹⁸ described instances in which hemorrhagic diarrhea and stomatitis occurred in conjunction with the hemorrhagic nephritis. Bory¹⁴ mentioned that Nichols reported a case of hemorrhagic nephritis following administration of bismuth in a patient with 'hypertensive Bright's disease'.

Most writers seemed to feel that the hemorrhagic nephritis was simply an expression of a local purpuric condition of the kidneys most likely accompanied by toxic nephrosis rather than a true hemorrhagic nephritis.

7 Catzeffis, A. A propos de trois préparations bismuthiques, tartrobismuthate de soude et de potasse, luatol, et iodobismuthate de quinine, *Ann d mal vén* 19:265-270, 1924.

8 Fournier, A. Accidents de la bismuthérapie, *Marseille méd* 63:1718-1733, 1926.

9 Gate, M. J. Les accidents de la médication bismuthique dans le traitement de la syphilis, *Vie méd* 8:357-359, 1927.

10 Dowds, J. H. Poisoning by Sodium Bismuth Tartrate Injections, *Lancet* 2:1039-1040, 1936.

11 Schröder, P. Ueber Nierenschädigungen bei der Wismutbehandlung bei Syphilis, *Zentralbl f inn Med* 52:498-501, 1931.

12 Leff, C. O. Chronic Bismuth Poisoning, *Mil Surgeon* 70:456-461, 1936.

13 Galliot, A. La bismuthothérapie. Incidents, accidents, intolerance, *J de med et chir prat* 106:639-644, 1935.

14 Bory, L. Néphrites bismuthiques, *Paris méd* 1:221-227, 1931.

15 Eitzen, A. C. Toxic Effects of Bismuth, with Especial Reference to Renal Damage and Report of a Case of Anuria, *Am J Syph, Gonorr & Ven Dis* 21:674-678, 1937.

16 Galliot, A. Mort par néphrite hémorragique au cours d'un traitement bismuthé, *Bull Soc franç. de dermat et syph* 34:174-176, 1927.

17 Gawalowski, K. Therapeutic Intoxication with Bismuth, *Česka dermat* 8:241-244, 1927.

18 Dassen, R., and Rey, J. C. Intoxicación aguda por el bismuto, *Semana méd* 2:1152-1156, 1930.

REPORT OF CASE

L B, a Negress aged 39, was first seen on June 18, 1936

Her husband had received a series of injections "for his blood" three years previously. The patient had never been pregnant, although she had been married fourteen years. There was a history of several attacks of "hives" many years before and of a tonsillectomy in her youth for recurrent sore throats. No evidence of constitutional or allergic diseases could be elicited either in the family history or in her past history.

Between October 1933 and March 1936 she received about forty-five "arm injections for bad blood." At some time during this period she received six injections in the buttocks. About nine months before her treatment terminated she had suffered nausea, chills and fever, but she was unable to state whether these symptoms occurred at the time of the intramuscular or the intravenous therapy. At any rate, it was quite clear that the patient tolerated the "arm treatments" without difficulty during the last nine months of the treatment.

A physical examination gave completely negative results. The Kahn and Kolmer serologic reactions and the result of an examination of the spinal fluid were reported as normal.

Treatment was begun on July 10, 1936, with intramuscular injections of 2 cc of bismuth subsalicylate in oil (120 mg of bismuth).

After both the fifth and the sixth injection the patient complained of itching, nausea, bad taste and headache, but after two weeks of rest the itching had almost entirely disappeared. The seventh and the eighth injections were tolerated well, but after the ninth and tenth treatments (October 16) the itching again became aggravated, and there developed a severely pruritic eruption, consisting of papules and vesicles scattered over the arms and the thighs and an erythematous edema involving the eyelids, the sides of the neck and the volar aspect of the left forearm. Bismuth medication was permanently discontinued.

By November 2 the eruption had become generalized and was strikingly polymorphous, and the vesicular and bullous phases were more pronounced. Ten days later the patient had become febrile and was ill enough to be admitted to the Hospital of the University of Pennsylvania.

At the time of her admission the patient presented an extensive generalized eruption consisting of erythematous, urticarial, vesicular and bullous lesions, of which some were grouped, some confluent and others discrete. Many of the lesions were oozing. Some of them presented annular and gyrate configurations. The face was the least involved, but the eyelids were swollen and the lips were studded with vesicles. Similar lesions were found at the angles of the mouth. The neck was heavily involved with erythematous patches and vesicular lesions. The extremities were swollen and tender and were the sites of confluent, oozing, eczematoid lesions, as well as erythematous, papular, vesicular and bullous lesions. On the trunk many of the lesions were urticarial, with superimposed vesicular and bullous elements.

Examination of the mouth revealed many filled and several capped teeth. The remainder of the physical examination gave negative results. The blood pressure was 120 systolic and 70 diastolic.

By November 15 the eruption had changed somewhat. Nearly all the elementary lesions had become large, clear, serous bullae, which arose from what appeared to be normal skin, but within one week they became hemorrhagic, and at the same time hemorrhagic erosive lesions formed in the nasal chambers and on the lips. This severe hemorrhagic phase continued for about five days, after which the patient's cutaneous condition began to improve.

During the first two weeks in the hospital the patient's general condition became gradually worse. She suffered greatly with nausea and frequent vomiting. There then ensued increasing weakness, dyspnea, abdominal distention and frequency of urination. The temperature by mouth ranged irregularly between 97 and 102 F, while the pulse and respiratory rates were more or less commensurate with the febrile changes.

Between December 1 and December 8 the patient was acutely ill. Although the temperature range remained about the same, the pulse and respiratory rates became rapid, 100 to 140 for the former and as high as 48 for the latter. At this time the patient complained of substernal pain, dyspnea and cough, all of great severity. Many rales were easily heard over the areas of both lungs, anteriorly and posteriorly. The picture was interpreted as diffuse bronchitis complicated by beginning cardiac failure. The rales disappeared in a few days but were succeeded by orthopnea, pallor, generalized edema and ascites. A gallop rhythm was present.

By December 4 it became evident that the patient also had acute nephritis. The urea nitrogen content of the blood had risen to 60 mg per hundred cubic centimeters, and red cells, albumin and casts made their appearance in the urine. The blood pressure rose to 160 systolic and 100 diastolic.

Several days later symptomatic evidences of improvement commenced. The dyspnea gradually subsided, the edema began to disappear, and the urinary output increased. Within ten days the urea nitrogen content of the blood fell to 18 mg per hundred cubic centimeters. All evidences of edema disappeared by December 29, and by Jan 8, 1937, the blood pressure reading had fallen to 132 systolic and 82 diastolic. The temperature, the pulse rate and the respiratory rate gradually reached normal and remained at these levels.

The patient was discharged from the hospital on January 26 and was observed regularly at the renal disease and dermatologic clinics. For a number of months after discharge the urinalyses continued to show decreasing numbers of red cells. These eventually disappeared entirely. Urinalyses in the past two years have given normal results.

During the height of the eruption a culture of the fluid taken from a newly formed bulla and a culture of the blood were both sterile under both aerobic and anaerobic conditions. A culture of the urine showed a few hemolytic staphylococci, while a culture of the substance taken from the root of a tooth extracted just before the patient left the hospital showed two types of nonhemolytic streptococci and some diphtheroids.

The patient's serum was tested with several strains of stock hemolytic streptococci in the laboratory of Dr Stewart Mudd by Dr D Sargeant Pepper, but no agglutinative power was demonstrated. Examination of the urine for bromides and iodides gave negative results on two occasions.

EXPERIMENTAL STUDIES

Vaccines were made with the organisms recovered from the extracted tooth and from the urine. A separate intracutaneous test of 0.1 cc was made for each type of organism recovered. None of these showed immediate or delayed reactions which were significantly more pronounced than the reaction caused by a control injection of stock catarrhal vaccine.

A report on the analysis of the preparation of bismuth subsalicylate in oil used on this patient was obtained from the manufacturer,¹⁹ who stated that it consisted of a suspension of bismuth subsalicylate in pure peanut oil. It contained in addition butyn 0.1 per cent and metaphen 1:10,000.

TABLE 1—*Intracutaneous and Passive Transfer Tests*

Substance Tested	Intracutaneous Tests				Prausnitz-Kustner Tests*			
	Subject		Control		Subject		Control	
	20	48	20	48	20	48	20	48
	Minutes	Hours	Minutes	Hours	Minutes	Hours	Minutes	Hours
Bismuth potassium tartrate (1 per cent)	14 by 13†	13 by 10	14 by 11	12 by 11	14 by 13	13 by 10	14 by 11	10 by 11
Neosarsphenamine (1 per cent)	12 by 8	7 by 8	11 by 11	8 by 7	11 by 10	7 by 8	10 by 12	8 by 6
Bismuth salicylate (1 per cent suspension)	7 by 5	3 by 3	8 by 6	8 by 6	6 by 4	3 by 3	8 by 6	7 by 5
Peanut oil	14 by 11	15 by 15	14 by 10	15 by 12	10 by 8	0	14 by 10	15 by 10
Butyn (1:1,000)	12 by 9	0	10 by 10	0	11 by 9	0	12 by 8	0
Metaphen (1:10,000)	8 by 8	6 by 6	11 by 11	6 by 5	12 by 8	6 by 6	11 by 9	6 by 5
Sodium salicylate (1 per cent)	8 by 8	2 by 2	11 by 19	2 by 2	11 by 8	2 by 2	11 by 8	2 by 2
Sodium tartrate (1 per cent)	13 by 9	2 by 2	11 by 8	2 by 2	11 by 9	2 by 2	11 by 8	2 by 2
Saline solution	8 by 9	0	10 by 10	0	8 by 11	2 by 2	10 by 11	0
Control serum					0	0	0	0

* Intracutaneous tests used as controls for Prausnitz-Kustner tests

† Size of papules recorded in millimeters

TABLE 2—*Intracutaneous Tests with Compound Antigen*

Substance Tested	Comp. Antigen Made with Subject's Serum				Comp. Antigen Made with Control Serum			
	Subject		Control†		Subject		Control†	
	20	48	20	48	20	48	20	48
	Minutes	Hours	Minutes	Hours	Minutes	Hours	Minutes	Hours
Bismuth tartrate (1 per cent)	8 by 5	8 by 5	8 by 6	8 by 6	6 by 3	6 by 3	6 by 5	6 by 5
Neosarsphenamine (1 per cent)	0	0	0	0	0	0	0	0
Bismuth subsalicylate in oil	8 by 6	8 by 6	9 by 6	9 by 6	8 by 5	8 by 5	10 by 6	10 by 6
Peanut oil	0	0	10 by 13	10 by 13	0	0	11 by 14	11 by 14
Subject's serum	0	0	0	0	0	0	0	0
Control serum	0	0	0	0	0	0	0	0

* The antigen was made by incubating equal parts of the test substance and the serum for twenty-four hours at 37°C.

† The intracutaneous tests in table 1 were used as controls.

We obtained samples of each of these constituents from the manufacturer and with these proceeded to perform a number of patch, intracutaneous (table 1) and passive transfer tests (table 1), which were carried out in duplicate on the patient and a control subject.

19 This report was submitted to us by Dr. G. W. Raiziss of the Dermatologic Research Laboratories in Philadelphia, a division of the Abbott Laboratories.

All these tests gave negative results in so far as they might demonstrate increased reaction capacity of the patient to the substances used

Table 2 is an attempt to demonstrate the reactivity of the skin to a compound antigen, made by incubating a double strength concentration of the test substance with equal parts of the serum obtained from either the patient or the control subject. The mixture was incubated at 37 F for twenty-four hours, and then 0.1 cc was injected intracutaneously.

By a comparison of these figures with results obtained from the simple intracutaneous tests as recorded in table 1, which were used as controls, it is obvious that no effective compound antigen was demonstrated.

The degrees of reactivity noted were the same irrespective of the serum used.

COMMENT

Pemphigoid or bullous toxic eruptions, like other toxic manifestations of the skin, may be caused by widely different etiologic agents. Certain drugs, notably the iodides, phenolphthalein, aconite,²⁰ antipyrine and arsenic,²¹ are well known for their tendency to produce this type of eruption in suitably sensitized persons. Recently the arsphenamines²² have also been incriminated in this respect. A not inconsiderable number of writers have reported similar eruptions in association with severe constitutional disorders, such as malignant conditions²¹ and acute infections.²³

It is generally agreed that one cannot prove that a drug is the cause of a particular eruption unless one can reproduce the eruption by subsequent administration of the suspected drug.²⁴ Such a procedure in the case of mild cutaneous manifestations is indeed feasible and is constantly being utilized to prove the causation of these conditions.

In regard to severe and dangerous types of eruptions, such as that in our patient, one is hardly justified in attempting to reproduce a con-

20 Fox, E. C. *Dermatitis Medicamentosa*, Dallas M. J. 18:138-139, 1932.

21 Elliot, J. A. *Bullous Dermatoses of Toxic Origin*. Report of a Case Involving an Association with Choriocarcinoma, Arch. Dermat. & Syph. 37:219-233 (Feb.) 1938.

22 (a) Muir, K. B. *Vesiculobullous Dermatitis Following Administration of Arsphenamine*. Case, Arch. Dermat. & Syph. 35:226-230 (Feb.) 1937. (b) Raubitschak, F. *Bullose Salvarsandermatose*, Arch. f. Dermat. u. Syph. 175:114-116, 1937.

23 (a) Roper, C. *Bullose hamorrhagische Dermatoze bei Typhus*, Munchen med. Wchnschr. 78:2036-2037, 1937. (b) Baryer, E. S., and Matveev, S. G. *Vesico-Bullous Hemorrhagic Dermatitis in Human Undulant Fever*, Sovet vrach gaz. 31:631-632, 1932. (c) Jona, G. *Su due casi di affezioni bullose fibrili*, Pediatria d. med. prat. 7:94-102, 1932.

24 Abramowitz, E. W. *Cardinal Points in the Diagnosis of Drug Eruptions*, M. Clin. North America. 22:1323-1331, 1938.

dition which on a previous occasion nearly resulted in the person's death Abramowitz²⁴ stated, "If it is not safe to use even the smallest dose of the suspected drug, then future avoidance of the particular drug, with actual use of the other drugs taken as a control should finally determine the one which is responsible"

Such a procedure was adopted in the case reported here After her recovery, the patient was given successively intramuscular injections of 2 cc each of peanut oil, butyn 0.1 per cent and metaphen 1:10,000, with no ill effects Furthermore, the patient was observed for a period of almost three years after her recovery, with no recurrence of her symptoms

The difficulties of proving a drug to be the cause of an eruption are complicated by the fact that, although a drug may be responsible for the occurrence of a dermatitis on one occasion, at some later time administration of the drug may fail to reproduce the eruption This situation seems to be particularly true of bismuth eruptions²⁵

It is, of course, well known that bismuth eruptions are much more common when there is previous or concomitant arsenical treatment than if a bismuth compound is administered alone²⁵ It seems as if arsphenamine sets the state or primes the patient for reactivity to bismuth Such might have been the situation with our patient

By following the arsenic-free technic of Schoch²⁶ in the routine cleansing of our syringes, we feel that an arsenical played no direct role in precipitating this patient's eruption

We were informed by the manufacturer that the bismuth compound which we used was free of any trace of arsenic, and this is borne out by reports in the literature,²⁷ which indicate that a great many bismuth preparations on the market today contain no trace of arsenic

25 (a) Sézary, A Les complications cutanées du traitement conjugué arsénobismuthique, *Progrès méd* 44:1891-1892, 1929 (b) Jordan, J W, and Walker, H L Dermatitis Due to Bismuth Compounds Associated with Cutaneous Sensitivity to the Arsenobenzols, *New York State J Med* 38:483-488, 1938 (c) Skolnick, E A, and Aleshire, I Skin Eruptions from Bismuth Therapy in Syphilis, *J A M A* 98:1798-1801 (May 21) 1932 (d) Grund, J C Bismuth Eruptions Disorders of the Skin Following Intra-Muscular Administration of Bismuth Compounds in Treatment of Syphilis, *Boston M & S J* 196:996-1000, 1927 (e) Lortat-Jacob, L, and Roberti, J Les érythrodermies bismuthiques, *Médecine* 8:147, 1926

26 Schoch, A G The Patch Test and the Element of Syringe Contamination in Arsphenamine Sensitization Dermatitis, *J A M A* 98:1367-1372 (April 16) 1932

27 (a) Lowenburg, H, and Naide, M Arsenic Poisoning Caused by a Mouth Wash Containing Solution of Potassium Arsenite, *J A M A* 100:737-738 (March 11) 1933 (b) Russel, E R Presence of Arsenic in Bismuth Preparations, *Arch Dermat & Syph* 28:841-842 (Dec) 1933

It has been repeatedly demonstrated in the literature on drug eruptions that the ordinary patch, intracutaneous and passive transfer tests usually fail to show the presence of sensitivity. As one would expect, our results with these procedures were entirely negative.

In accordance with the fundamental work of Landsteiner²⁸ on conjugated antigens and its application by Rosenthal²⁹ to the experimental demonstration of the transfer of phenolphthalein sensitivity by means of a phenolphthalein conjugate, we attempted to demonstrate sensitivity to an incubated mixture of serum and bismuth which presumably might contain an appropriate compound antigen. These experiments all gave negative results.

Kenedy³⁰ reported that he was able to demonstrate the passive transfer of phenolphthalein sensitivity by performing the Prausnitz-Kustner test on a normal person who previously had ingested phenolphthalein. He stated the belief that the normal control subject elaborated the appropriate compound antigen, which in turn reacted with the antibodies in the serum of the sensitive person, thus resulting in a positive reaction.

It was because of Kenedy's work that we chose as our control subject a person who was receiving, but who showed no evidences of reactivity to, bismuth subsalicylate in oil. We, however, were unable to repeat Kenedy's results.

There is much evidence that this patient had true hemorrhagic nephritis rather than a purpuric manifestation with nephrosis. In the first place, the red cells appeared in the urine after the hemorrhagic phenomena in the skin and mucous membranes had disappeared. Furthermore, red cells as well as casts and albumin were found in the urine for several months after the patient's discharge from the hospital. At the time of the onset of the urinary changes there were not only anemia and increased blood urea nitrogen but also a rise in blood pressure.

It may be, as Bory¹⁴ stated, that a toxic condition, such as this patient presumably had, may precipitate a potentially primed but latent hemorrhagic nephritis into activity. Stokes and Cathcart³¹ have pointed out the role that infection plays in precipitating outbreaks of allergic

28 Landsteiner, K. *Specificity of Serological Reactions*, Springfield, Ill., Charles C. Thomas, Publisher, 1936, p. 100.

29 Rosenthal, S. R. *The Conjugation of Haptens in Vivo*. Phenolphthalein, *J. Immunol.* **34**: 251-267, 1938.

30 Kenedy, D. *Sulla ipersensibilità alla fenolftaleina*, *Gior. ital. di dermat. e sif.* **75**: 965-968, 1934.

31 Stokes, J. H., and Cathcart, E. P. *Contributory Factors in Post-Arsphenamin Dermatitis*, *Arch. Dermat. & Syph.* **7**: 14-49 (Jan.) 1923.

character Also, the biotropism of Milian³² has been broadened to include this type of reactivity For this reason, we studied the reactions to the intracutaneous injection of organisms which were cultured from the abscessed tooth and from the urine in the hope of demonstrating increased reactivity, but the results of the tests were all within normal limits Similarly, the agglutination tests of the patient's serum to various strains of stock streptococci gave negative results

SUMMARY

A case is reported in which a generalized bullous eruption and hemorrhagic nephritis followed bismuth therapy In the literature no other case of a similar nature has been reported Various tests to demonstrate objectively sensitivity to bismuth all gave negative results Our reasons for believing that this patient's symptoms were due to reactivity to bismuth are discussed

³² Milian, G, in Darier, J, and others *Nouvelle pratique dermatologique*, Paris, Masson & Cie, 1936, vol 4, p 688

A PROPOSED CLASSIFICATION OF CUTANEOUS LIPOIDOSES

WITH DESCRIPTION OF A NEW LOCAL LIPOID DERMATOSIS IMBIBITIO
LIPOIDICA COLLAGENI DEGENERATI CUTIS

ERICH URBACH, M D

AND

WILLIAM R HILL, M D

PHILADELPHIA

The lipoidoses, as one of us (E U) explained elsewhere,¹ are now classified in two large groups, namely, the general and the local lipoidoses. This division is based on demonstration of the fact that in the former there is a general, primary disturbance of fat metabolism, whereas in the latter there is a local disease of the tissue with secondary deposition of fat.

The general lipoidoses represent a process of fatty infiltration, their further classification is based on clinical type, the nature of the lipoid (cholesterol ester, free cholesterol, phosphatide, lecithin or kerafin), the intracellular or extracellular presence of the lipoid and the histologic features. The table presents a summary of these items.

The xanthelasmatoses (this term is preferable to xanthoma, because a blastomatous character is demonstrable only in extremely rare instances) can at present be classified only from a clinical point of view, because histologically and chemically no sharp differentiation is possible.

- (1) Xanthelasma
 - (a) xanthelasma localisatum (xanthelasma palpebrae and xanthelasma tumoriforme)
 - (b) xanthelasma disseminatum
 - (c) xanthelasma diffusum (cholesteroderma, complete infiltration of extensive areas)
 - (d) xanthelasma generalisatum (including involvement of the mucosae and internal organs)Special type Hand Schuller Christian syndrome
- (2) Xantheloid (formerly designated xanthofibroma and xanthofibrosarcoma)
- (3) Xanthoma (xanthoblastoma)

The local lipoidoses are caused by primary local disease of the tissue of most varied nature (trauma, infection, intoxication or wear and tear) with a secondary deposition of lipoid in the involved tissue. We have earlier designated this process as "imbibition," in order to emphasize what will be discussed more fully, namely, that we have here to deal

From the Department of Dermatology and Syphilology University of Pennsylvania, School of Medicine, John H. Stokes, M D, Director

1 Urbach, E. Lipoid Stoffwechselerkrankungen der Haut, in Jadassohn, J. - Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer 1932, vol 12, p 238

with not lipid degeneration of the connective or elastic tissue but impregnation of primarily diseased tissue with fatty substances excreted by the blood at this site. The question as to whether disturbed local fat metabolism or increased blood lipid must be considered as a necessary prerequisite would have to be answered differently for the various local lipid dermatoses, i. e., the blood lipid is normal in cases of resorption

Proposed Classification of the Cutaneous Lipoidoses (Urbach)

Lipoidoses	Clinical Type	Type of Lipoidosis, as Regards Histologic and Chemical Nature	Chief Chemical Characteristics
General	Xanthelasmatosi (infiltration type)	Cholesterol cellular lipoidosis	Cholesterol ester and free cholesterol (ratio 2:1)
	Extracellular cholesterosis (Urbach, Epstein and Lorenz ⁴¹ , Kerl, W., in Jadassohn, J., and Zeller, K. <i>Iconographia der matologica</i> , Berlin, Urban & Schwarzenberg, 1932)	Cholesterol lipoidosis	Free cholesterol and cholesterol ester (ratio 3:1)
	Niemann Pick disease	Phosphatide cellular lipoidosis	Leathin
	Hepatosplenomegalic skin and mucous membrane lipoidosis (Burger, M., and Grütz, O. <i>Arch f Dermat u Syph</i> 166: 542, 1932)	Phosphatidic and phosphatide cellular lipoidosis	Phosphatides and cholesterols
	Lipoid proteinosis (Urbach, E., and Wiethe, C. <i>Virchows Arch f path Anat</i> 273: 585, 1929, <i>Arch f Dermat u Syph</i> 168: 94, 1933)	Phosphatidic lipoidosis	Lipoid protein mixture, the former probably from the phosphatide group
	Gaucher's disease	Cerebroside cellular lipoidosis	Kerasin
Local	Xanthelasma (resorption type) (Urbach, E. <i>Klin Wehnschr</i> 2: 542, 1923)	Cholesterol cellular lipoidosis	Cholesterol ester and free cholesterol (ratio 2:1)
	Necrobiosis lipoidica diabeticorum (Urbach ⁴² and Oppenheim ⁴³)	Lipoid imbibition of primarily necrotic cutaneous tissue	Lipoids not belonging to the cholesterol group
	Imbibitio lipoidica telae elasticae degeneratae	Lipoid imbibition of pathologically altered elastic tissue of the skin	Lipoids not belonging to the cholesterol group
	Imbibitio lipoidica collageni degenerati cutis	Lipoid imbibition of pathologically altered connective tissue of the skin	Lipoids not belonging to the cholesterol group

xanthelasma and imbibitio lipoidica telae elasticae degeneratae but increased in cases of necrobiosis lipoidica diabeticorum and of imbibitio lipoidica collageni degenerati cutis

Among the local lipoidoses one also has to distinguish several diseases, as shown in the table, in part depending on the chemical aspects of the lipoids but predominantly, however, according to the tissues in which imbibition occurs (connective tissue, elastic tissue and necrotic tissue)

Certain objections have been offered to our classification. Andrews² has described it as "Slightly arbitrary, because the chemical nature of some of the lipoids is extremely complex and as yet not understood." He furthermore demurred that "There seems to be a mixture of several types." Weidman³ most justly has stipulated that only the future will show whether this classification will prove merely transitory or permanent, for at the date of that criticism there had appeared few, if any, confirmations of the new disease pictures presented by one of us (E. U.), such as extracellular cholesterosis, lipoid proteinosis and necrobiosis lipoidica diabetorum. Fortunately, in the meantime numerous writers from various countries have reported a large number of such cases, the most important of the writers are listed in the following tabulation.

Extracellular Cholesterosis		
Laymon ⁴	} The articles refer to the same case	
Montgomery and Osterberg ⁵		
Lipoid Proteinosis		
Benesi ⁶		Wise and Rein ¹¹
Hoffmann ⁷		Havthausen ¹²
Kindler ⁸		Bazex ¹³
Tripp ⁹		Hansen ¹⁴
Schreus ¹⁰		
Necrobiosis Lipoidica Diabeticorum		
Galewsky ¹⁵	Monacelli ²³	Bernstein ²²
Balbi ¹⁶	Kren ²⁴	Greenwood and Rockwood ²⁵
Gotttron ¹⁷	Connor ²⁶	Swetzer and Laymon ²⁴
Zelsler and Oaro ¹⁸	Nicolau ²⁰	Fox ²⁵
Michelson and Laymon ¹⁹	Klaber ²⁷	Wile and Belote ²⁶
Tannenholz ²⁰	Usher and Rabinowitch ²⁸	Rattner ²⁷
Goldsmith ²¹	Jamieson ²⁹	Riehl ²⁸
Gross and Machacek ²²	Swetzer ³⁰	Boldt ²⁹
	Hitch ³¹	Schuermann ³⁰

2 Andrews, G. C. *Diseases of the Skin*, Philadelphia, W. B. Saunders Company, 1938.

3 Weidman, F. D. Position of "Pseudodiabetic Xanthoma" Among the Lipoid Disturbances of the Skin (Urbach), *Arch. Dermat. & Syph.* **35**: 815 (May) 1937.

4 Laymon, C. W. Extracellular Cholesterosis, *Arch. Dermat. & Syph.* **35**: 269 (Feb.) 1937.

5 Montgomery, H., and Osterberg, A. E. Xanthomatosis, *Arch. Dermat. & Syph.* **37**: 373 (March) 1938.

6 Benesi, O. Zur Kenntnis der Lipoidosis cutis et mucosae (Urbach und Wiethe), *Ztschr. f. Laryng., Rhin. u. Otol.* **21**: 60, 1931.

7 Hoffmann, E. Lipoidosis cutis et mucosae, *Dermat. Ztschr.* **62**: 296, 1931.

8 Kindler, W. Beitrag zur Lipoidosis cutis et mucosae (Lipoidproteinose), *Ztschr. f. Hals-, Nasen- u. Ohrenh.* **30**: 659, 1932.

9 Tripp, R. N. Lipoidosis Cutis et Mucosae, *New York State J. Med.* **36**: 619, 1936.

10 Schreus, H. T. Lipoidproteinose Urbach Wiethe, *Zentralbl. f. Haut- u. Geschlechtskr.* **53**: 529, 1936.

Nearly all these authors at the time of writing were of the opinion that the aforementioned lipid dermatoses had been clearly defined histologically and clinically so as to justify their special designation and differentiation

11 Wise, F, and Rein, C R Lipoidosis Cutis et Mucosae (Lipoid-Proteinosis of Urbach), Arch Dermat & Syph **37**:201 (Feb) 1938

12 Haxthausen, H Lipoidosis cutis et mucosae (Urbach), Zentralbl f Haut- u Geschlechtskr **55**:514, 1937

13 Bazex, A Un cas de lipoido-proteinose (Maladie de Urbach-Wiethe), Bull Soc franç de dermat et syph **46**:136, 1939

14 Hansen, P. Ein Fall von Lipoidproteinose, Arch f Dermat u Syph **175**:618, 1937

15 Galewsky, E Nekrobiosis lipoidica diabetorum (Urbach), Zentralbl f Haut- u Geschlechtskr. **43**:252, 1933

16 Balbi, E Ricerche intorno alla patogenesi della necrobiosis lipoidica diabetorum Urbach-Oppenheim, Gior ital di dermat e sif **74**:14, 1933

17 Gottron, H. (a) Dermatitis atrophicans lipoides diabetica, Zentralbl f Haut- u Geschlechtskr **43**:721, 1933, (b) Zur Kenntnis und Pathogenese der Dermatitis atrophicans lipoides diabetica bzw Nekrobiosis lipoidica diabetica, Med Klin **34**:145 and 190, 1938

18 Zeisler, E P, and Caro, M R Nekrobiosis lipoidica diabetorum, Arch f Dermat u Syph **30** 796, 1934

19 Michelson, H E, and Laymon, C W Necrobiosis Lipoidica Diabeticorum (Urbach) Dermatitis Atrophicans Lipoides Diabetica (Oppenheim), J A M A **103**:163 (July 21) 1934, Necrobiosis Lipoidica Diabeticorum, Arch Dermat & Syph **35**:1130 (June) 1937

20 Tannenholz, H Necrobiosis Lipoidica Diabeticorum (Urbach), Arch Dermat & Syph **29**:931 (June) 1934

21 Goldsmith, W N. Necrobiosis Lipoidica, Proc Roy Soc Med **28**:363, 1935

22 Gross, P, and Machacek, G F Necrobiosis Lipoidica Diabeticorum, Arch Dermat & Syph **32**:491 (Sept) 1935

23 Monacelli, M A proposito di lipoidosi cutanee, Boll sez region Soc ital di dermat e sif (supp, Gior ital di dermat e sif), 1935, no 3, p 212

24 Kren, O Necrobiosis lipoidica diabetorum, Zentralbl f Haut- u Geschlechtskr **49**:581, 1935; **55**:186 and 614, 1937

25 Connor, W H Necrobiosis Lipoidica Diabeticorum, Arch Dermat & Syph **34**:705 (Oct) 1936

26 Nicolau, S Ein Fall von Nekrobiosis lipoidica diabetorum (Oppenheim-Urbach), Zentralbl f Haut- u Geschlechtskr **53**:373, 1936, **57**:578, 1938

27 Klaber, R Necrobiosis Lipoidica Diabeticorum (Urbach-Oppenheim), Proc Roy Soc Med **27**:713, 1934, **30**:976, 1937

28 Usher, B, and Rabinowitch, I M Necrobiosis Lipoidica Diabeticorum, Arch Dermat & Syph **35**:180 (Jan) 1937

29 Jameson, R C Necrobiosis Without Diabetes, Arch Dermat & Syph **36**:912 (Oct) 1937, Necrobiosis Lipoidica Diabeticorum, *ibid* **38**:311 (Aug) 1938

30 Sweitzer, S E Necrobiosis Lipoidica Diabeticorum, Arch Dermat & Syph **37**:150 (Jan) 1938

(Footnotes continued on next page)

EXTRACELLULAR CHOLESTEROSIS

It was only in the consideration of extracellular cholesterosis that Montgomery and Osterberg⁵ suggested its classification as a form of xanthelasma (xanthoma) or xantheloid (xanthofibroma). The four chief points of differentiation between extracellular cholesterosis and xanthelasmatis, in order to make the distinction between them perfectly clear, are the following:

1 *Clinical Picture*—The clinical picture and course of extracellular cholesterosis are characteristic. The disease begins as an exanthem in the form of an erythema exsudativum multiforme. In both cases hitherto described (Urbach,⁴¹ Laymon⁴ and Montgomery and Osterberg⁵) vesicular primary efflorescences were demonstrated clinically and histologically. To date such lesions have not been described in cases of xanthelasma or xantheloid.

2 *Histologic Picture*—Histologic examination reveals changes in efflorescences only a few days old, as well as in apparently normal skin, indicating primary injury of the epithelium and vessels at a time when the rest of the cutaneous tissue has a normal histologic appearance. Besides this severe injury of the vascular endothelium, after staining with sudan the walls of nearly all the capillaries show brownish red deposits, which as yet show no double refraction. As, however, aciculae and specks appear in the vicinity of the brown-stained areas on addition

31 Hitch, J. M. Necrobiosis Lipoidica Diabeticorum (Urbach and Oppenheim), Arch Dermat & Syph 36 536 (Sept) 1937

32 Bernstein, J. C. Necrobiosis Lipoidica Diabeticorum (Urbach), Arch Dermat & Syph 36 282 (Aug) 1937

33 Greenwood, A. M., and Rockwood, E. M. Necrobiosis Lipoidica Diabeticorum, Arch Dermat & Syph 35 727 (April) 1937

34 Sweitzer, S. E., and Laymon, C. W. Necrobiosis Lipoidica Diabeticorum, Arch Dermat & Syph 35 967 (May) 1937

35 Fox, H. Necrobiosis Lipoidica Diabeticorum, Arch Dermat & Syph 37 1072 (June) 1938

36 Wile, U. J., and Belote, G. Necrobiosis Without Diabetes, Arch Dermat & Syph 38 311 (Aug) 1938

37 Rattner, H. Necrobiosis Lipoidica Diabeticorum, Arch Dermat & Syph 38 268 (Aug) 1938

38 Riehl, G., Jr. Necrobiosis lipoidica diabeticorum, Zentralbl f Haut- u Geschlechtskr 57 11, 1938

39 Boldt, A. Nekrobiosis lipoidica (diabeticorum), Arch f Dermat u Syph 179 74, 1939

40 Schuermann, H. Nekrobiosis lipoidica ("Diabeticorum") ohne Diabetes im Bereiche einer Purpura Majocchi bei Hypertonus, Zentralbl f Haut- u Geschlechtskr 62 339, 1939

41 Urbach, E., Epstein, E., and Lorenz, K. Extrazelluläre Cholesterinose, Arch f Dermat u Syph 166 243, 1932

of digitonin at this time, it is assumed that the lipid substances are formed chiefly from free cholesterol

3 *Histochemical Picture*—Histochemical examination reveals an almost exclusively extracellular, i e, interfibrillar and intrafibrillar, distribution of the lipid substances. This leading symptom is in no way invalidated by the fact that here and there a histiocyte may absorb lipid, giving rise to foam cells.

4 *Chemical Findings*.—Chemical examination shows that the ratio of cholesterol fatty acid ester to free cholesterol in a xanthelasma nodule is 2:1, in extracellular cholesterosis the ratio is reversed, i e, 1:3.

For all these reasons, we believe that the syndrome which we have named extracellular cholesterosis must be differentiated from xanthelasmatoses and xantheloid and must be presented as an independent entity

NECROBIOSIS LIPOIDICA DIABETICORUM

In regard to the pathogenesis of necrobiosis lipoidica, opinions vary because some writers fail to attribute a determining significance to diabetes, as is done by Urbach⁴². Without entering into a polemical discussion, one of us (E U) wishes merely to draw attention to the fact that a normal result of a dextrose tolerance test does not necessarily exclude the former existence of diabetes. In this connection it must be recollected that xanthelasma may be associated with normal cholesterol content of the blood and that local myxedema of the skin may occur in hyperthyreosis.

For this reason, in cases of necrobiosis lipoidica with a negative result to a dextrose tolerance test, we recommend a determination of the sugar content of the skin or a cutaneous dextrose tolerance test (Urbach⁴³).

It may be possible, however, that necrobiosis lipoidica can develop on other than a diabetic-toxic basis. According to Urbach, this disease is caused by damage of the walls of the blood vessels by toxic substances, with consequent local circulatory disturbances leading to necrobiosis. Owing to imbibition of the necrobiotic tissue with fat from the blood, there develops a secondary clinical picture of necrobiosis lipoidica. According to whether diabetes or other causes are responsible for these vascular changes, one may therefore speak of necrobiosis lipoidica diabeticorum or necrobiosis lipoidica of some other origin.

42 Urbach, E. (a) Beiträge zu einer physiologischen und pathologischen Chemie der Haut. X. Mitteilung. Eine neue diabetische Stoffwechseldermatose. Necrobiosis lipoidica diabeticorum, Arch f Dermat u Syph 166:273-285, 1932, (b) Necrobiosis lipoidica diabeticorum mit Augenhintergrundveränderungen, Zentralbl f Haut- u Geschlechtskr 50:281, 1935.

43 Urbach, E. Zum Problem des isolierten hohen Hautzuckers bzw Hautdiabetes, Klin Wchnschr 16:452, 1937.

We are well aware of the difficulties associated with chemical confirmation of lipid mixtures. However, in the presence of unequivocal and characteristic results, such as decided predominance of free cholesterol as compared with the predominance of cholesterol ester or the demonstration of phosphatides or lipid-protein mixtures, these may even now be of value. These difficulties may become almost insurmountable if the diseased cutaneous areas are small, so that the biopsy specimen weighs only a few decigrams, as is the case with local lipoidoses. The histochemical methods are even less reliable, although a change in this regard may be brought about by the introduction of the use of fluorescence in microscopic technic.

In our opinion, there shortly will appear new lipid dermatoses, differing clinically, histologically and chemically from those previously described. The disease which we herein describe is such a new lipid dermatosis. It belongs to the so-called local lipoidoses and constitutes the fourth of this group that we have presented.

We understand the term "resorption xanthelasma" to mean a deposition of cholesterol fatty acid esters and free cholesterol in scars or otherwise injured cutaneous areas, associated with normal cholesterol metabolism. Whether in such cases the lipid substances are liberated by the pathologic process in the tissue or are derived from the blood cannot at present be stated. Weidman⁴⁴ has contributed an excellent study of this problem.

With regard to necrobiosis lipoidica diabetorum, differences in opinion might arise as to whether it would not more properly belong in the group of the general lipoidoses, because chemical analysis of the blood reveals hyperlipidemia and hypercholesteremia, when, in spite of this, the lipoidosis is classified in the group of local lipoidoses, it is done in consideration of the outstanding symptom of necrobiosis, which in our opinion constitutes the primary basis for the local lipid deposition. As is well known, there exists a wide difference between Oppenheim's⁴⁵ conception and our own,⁴² Oppenheim has assumed that lipid degeneration of the connective tissue is the cause of the yellow discoloration of the cutaneous lesions, whereas we assume that lipid imbibition of the primarily necrotic tissue is the cause. We have introduced the working hypothesis of lipid "imbibition" (deposition of lipid substances in a tissue primarily injured from other causes), because the

44 Weidman, F. D. The Pathology of the Yellowing Dermatoses, *Arch Dermat & Syph* 24 954 (Dec.) 1931.

45 Oppenheim, M. Ueber eine bisher nicht beschriebene, mit eigentümlicher lipoider Degeneration der Elastica und des Bindegewebes einhergehende chronische Dermatoze bei Diabetes mellitus (*Dermatitis atrophicans lipoides diabetica*), *Arch f Dermat u Syph* 166 576, 1932.

pathologic anatomists, according to von Gierke,⁴⁶ refute the concept of lipid degeneration of the connective and elastic tissues. Von Gierke wrote as follows: "The classification (fatty infiltration—fatty degeneration) corresponds to the theory that in infiltration the fat is carried from other parts of the body, but in degeneration is formed from decomposition of the cellular protein. This theory cannot be maintained, because we know now that also in fatty degeneration the fat is resorbed from the lymph current and because, on the other hand, it has not been possible to demonstrate any direct production of fat from protein in the animal or human body."

The significant difference lies only in the condition of the fat-containing cells, in the first case the condition is fatty infiltration of otherwise normal cells, whereas in the second case the condition is fatty infiltration of injured cells. In order to find expression for this in the nomenclature, one of us (E. U.)⁴² once suggested that the term lipid infiltration be used to designate fatty infiltration of otherwise normal cells or tissues and that the term lipid imbibition be used to designate fatty infiltration of diseased or injured cells or tissues. We chose the latter designation because, as is well known, pathologically changed tissue shows a decided tendency to imbibe all manner of substances excreted by the blood, such as calcium, iron or pigment. Also, the designation fat phanerosis cannot be accepted. This term is meant to convey the rendering visible of previously dissolved or invisible and finely distributed fat substances by droplet precipitation or confluence. We rejected the term principally because the fat deposition in the diseased tissues is derived most probably from the blood fats and not from the locally liberated fat.

But quite apart from the fact that the conception of lipid degeneration is not permissible from a pathologic anatomic standpoint, microscopic observation has shown that it would be most improbable in cases of necrobiosis lipoidica. With greater enlargement of specimens⁴⁷ stained with sudan, it can be shown that besides a diffuse brown staining of the basic substance, there is also striate or aciniform distribution of the lipid droplets, which could be produced only by deposition of lipid from without (via the blood stream) and never from local transformation of protein bodies into fatlike substances.

IMBIBITIO LIPOIDICA TELAE ELASTICAE DEGENERATAE

The same objections that we presented to Oppenheim's conception of necrobiosis hold good here with relation to a disease picture which

46 von Gierke, E. Störungen des Stoffwechsels in Aschoff, L. Pathologische Anatomie, Jena. Gustav Fischer, 1919, vol. 1, p. 429.

47 Urbach,^{42a} fig. 7, p. 280.

Kreibich⁴⁸ has named "lipoid degeneration of the elastin" We have been able to demonstrate rather that one has here to deal with a primary severe lesion of the elastic tissue, usually of the face or neck (due to senility, light or exposure), which assumed secondarily a yellow color due to deposition of locally liberated lipoids For these reasons we have suggested the designation "imbibitio lipoidica telae elasticae degeneratae"⁴⁹ This constitutes not so much a special clinical entity as a peculiar pathologic anatomic condition of various cutaneous lesions associated with a primary degeneration of the elastic tissues

IMBIBITIO LIPOIDICA COLLAGENI DEGENERATI CUTIS

In the following pages are described a new local lipoid dermatosis which we have named "imbibitio lipoidica collageni degenerati cutis" As can be gleaned from this name, the condition this time is lipoid imbibition that involves exclusively primarily diseased cutaneous connective tissue, whereas in the foregoing paragraphs we considered a disease that involved only the elastic tissue and in necrobiosis lipoidica diabetorum, primary local necrosis of all elements of the skin

REPORT OF CASES

CASE 1—V W,⁵⁰ an obese white woman aged 52, had about a dozen indurated lesions of diversified appearance on the external lateral surfaces of the arms, thigh and legs The latest lesion, which had been present on the external aspect of the left tibia for three years, was about 4 mm in diameter, elevated, hard and reddish brown The other lesions, varying in duration from ten to thirty years, were of three types All were definitely situated in the deeper part of the cutis, the skin over them being depressed and violet brown, they had a cartilaginous feel Other lesions, likewise situated deeply in the cutis, presented an elevated keloid-like surface Two lesions (above the right anterior iliac spine and on the left thigh) differed from all others in that they were yellowish brown but on pressure became distinctly yellow Clinically, these lesions resembled necrobiosis lipoidica diabetorum The patient had rheumatism at the age of 13, and after that she had five attacks about five years apart As a rule the attacks were limited to one joint, which became red and swollen, requiring rest in bed for one month for relief A tonsillectomy was performed nineteen years previously The first lesion (on the left hip) appeared thirty years ago, apparently associated with the rheumatic attack The other lesions appeared on the arms, legs and thighs at various intervals, usually about five years apart, the last three years ago None of the later lesions seemed to be related to the rheumatic infection There was no history of preceding trauma The blood pressure was 130 systolic and 70 diastolic The peripheral arteries showed no beading or abnormal tortuosity Except for slight

48 Kreibich, C Ueber lipoide Degeneration des Elastins der Haut, Arch f Dermat u Syph 116 325, 1913

49 Urbach, E Imbibitio lipoidica telae elasticae degeneratae, Acta dermat-venereol 15 69, 1934

50 Presented at a meeting of the Philadelphia Dermatological Society, May 19, 1939 (Arch Dermat & Syph 41.180 [Jan] 1940)

arteriosclerotic changes in the vessels, the eyegrounds appeared normal. The blood tests for syphilis gave negative results and the basal metabolic rate was +4 per cent. There were 5,000,000 red blood cells per cubic millimeter, with 7,200 white blood cells per cubic millimeter. Dextrose tolerance tests gave the following results:

Fasting	94
Half hour after ingestion of 100 Gm of dextrose	164
One hour after ingestion of 100 Gm of dextrose	121
Two hours after ingestion of 100 Gm of dextrose	104

For certain reasons only the blood serum of the patient was examined for cholesterol at the first examination:

Total cholesterol	362 mg per hundred cubic centimeters
Ester cholesterol	227 mg per hundred cubic centimeters
Free cholesterol	135 mg per hundred cubic centimeters

Immediately thereafter the patient was given a fat-free diet. The second determination of the principal lipid components was made three weeks later. The results of lipid analysis⁵¹ of the blood serum at this time, compared with normal values are as follows:

	Patient's Values Mg per 100 Cc	Normal Values Mg per 100 Cc
Total lipid	749	570 to 820
Neutral fat	200	100 to 200
Total fatty acids	413	190 to 420
(a) Phospholipid fatty acids	93	115 to 220
(b) Cholesterol ester fatty acids	131	64 to 88
(c) Neutral fat fatty acids	189	10 to 170
Total cholesterol	279	150 to 200
Ester cholesterol	196	90 to 130
Free cholesterol	83	70 to 90
Phospholipid phosphorus	5.6	7 to 14
Phospholipid as lecithin	140	175 to 330

It is clear that the original cholesterol level was considerably higher and was rapidly and greatly influenced by the fat-free diet. It also may be concluded, therefore, that the values of other fat components, all of which were found at the upper limits of normal, were probably increased before institution of the fat-free diet.

As the histologic findings in this case are identical with those in the second case, they will be considered with the latter.

CASE 2—S B, an obese Italian woman aged 48, was admitted to the hospital because of pruritus vulvae, which had been present for seven to eight years. The menopause occurred one year previously. On the external aspect of the upper part of the left arm was a yellowish red nodule about the size of a cherry, which, according to the patient, had been present for about thirty-seven years and had developed after vaccination. She was certain of this because she remembered that the nodule had itched and she had scratched it. The blood sugar value was 107 mg per hundred cubic centimeters. Blood tests for syphilis gave negative results.

⁵¹ Total cholesterol was determined by Bloor's method. Ester cholesterol was determined by Bloor's method. Phospholipid was determined by the Fiske-Subbarow method. Fatty acids were determined by Stoddard and Drury methods. All other values were calculated from these values, as described by E. M. Boyd (*The Oxidative Micro-Estimation of Blood Lipids*, *Am J Clin Path [Tech Supp]* 2.77, 1938).

The patient had suffered for fifteen years from pains in the upper part of the right side of the abdomen. The region of the gallbladder was sensitive to pressure.

The results of lipid analysis of the blood were as follows:

	Patient's Values Mg per 100 Cc	Normal Values Mg per 100 Cc
Total lipid	868	570 to 820
Neutral fat	325	100 to 200
Total fatty acids	540	190 to 420
(a) Phospholipid fatty acids	103	115 to 220
(b) Cholesterol ester fatty acids	128	04 to 88
(c) Neutral fat fatty acids	309	10 to 170
Total cholesterol	275	150 to 200
Ester cholesterol	192	90 to 130
Free cholesterol	83	70 to 90
Phospholipid phosphorus	6.8	7 to 14
Phospholipid as lecithin (lipoid phosphorus \times 25)	165	175 to 330

Histologic Study—Three nodules of various ages from case 1 (nodules of three, ten and thirty years' duration, respectively) and from the only tumor present in case 2, which was of thirty-seven years' duration, were studied histologically. The two last-mentioned tumors, which had persisted for at least three decades, presented identical pictures.

The most interesting and pathogenically the most important finding was that the histologic structure of all the tumors was practically the same except that in the younger nodules, of three to ten years' duration, no lipid deposition could be demonstrated. From this finding the important conclusion may be drawn that the condition could not be a primary lipid dermatosis but must be a local inflammatory lesion of the skin due to some other cause and proceeding to secondary lipid absorption.

Hematoxylin-Eosin and Trichrome Stain—More or less intense hyperkeratosis was present. The vessels in the stratum papillare cutis were dilated. Characteristic changes were seen in the connective tissue. In parts there appeared extraordinary proliferation of the connective tissue cells, with darkly staining nuclei and a striking diminution or condensation of the connective tissue fibrils (fig. 1). Among these, especially in the older nodules, there appeared abundant longitudinal cavities, which suggested that treatment of the sections with alcohol might have led to extraction of some substance, probably of a fatlike nature (fig. 2).

In other more deeply situated portions the connective tissue appeared condensed, consisting of irregular whorls (fig. 3).

The newly formed connective tissue showed extremely poor vascularization. The vessels that were present had thickened walls, with a swelling of the intimal cells.

Van Gieson's Stain—Those areas which in the hematoxylin-eosin or trichrome specimens appeared rich in cells and nuclei after staining with Van Gieson's stain became greenish yellow instead of bright red. Furthermore, the normal gross fascicular structure of the connective tissue was lacking and was replaced by a fine linear whorl configuration.

Weigert's Stain—This stain showed complete absence of elastic tissue, as regards both staining and structure in those portions of the skin which appeared yellow when the Van Gieson stain was employed.

Unna's Polychrome Methylene Blue Stain—The pathologic components of the cutis appeared blue, indicating a so-called basophilic degenerated collagen or elacin, according to Unna.

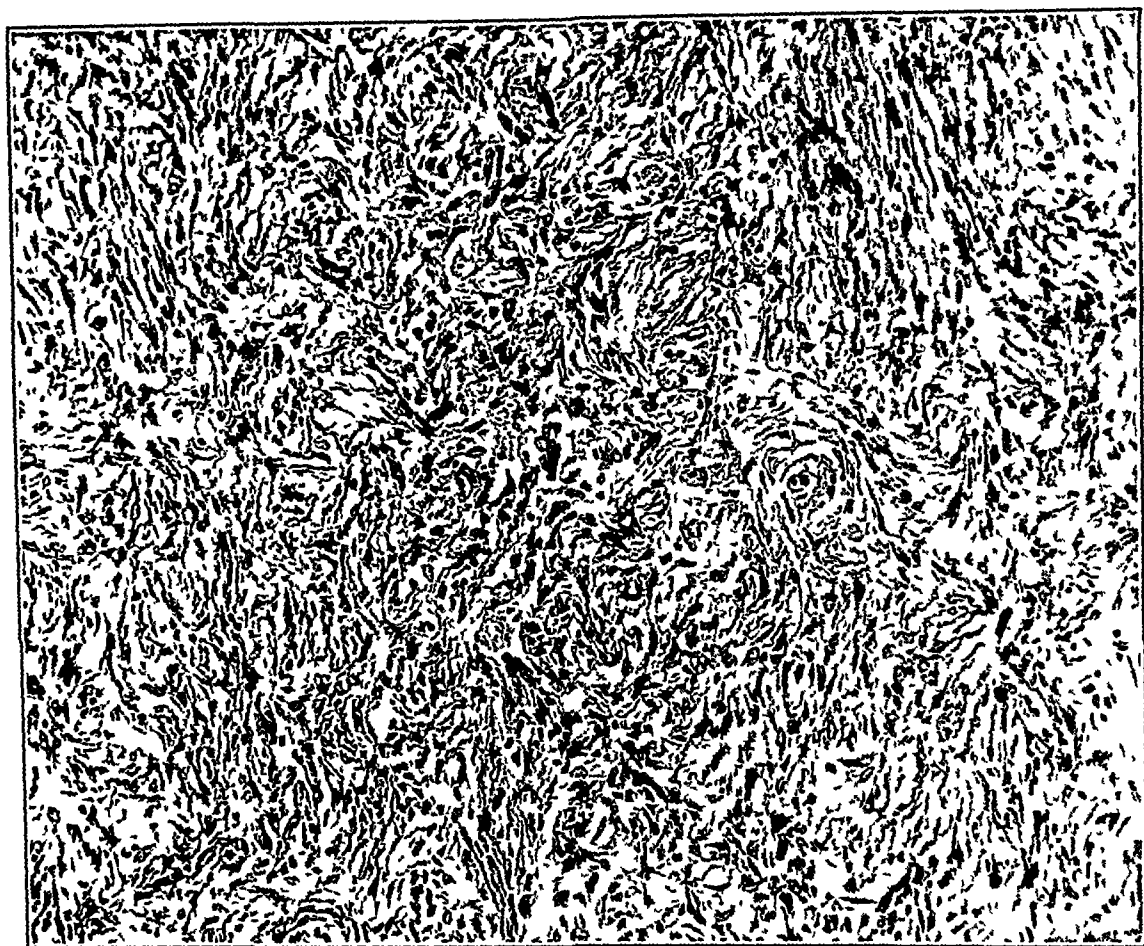


Fig 1—Extraordinary proliferation of the connective tissue cells, with darkly stained nuclei and condensation of the connective tissue fibrils (hematoxylin-eosin, $\times 132$)

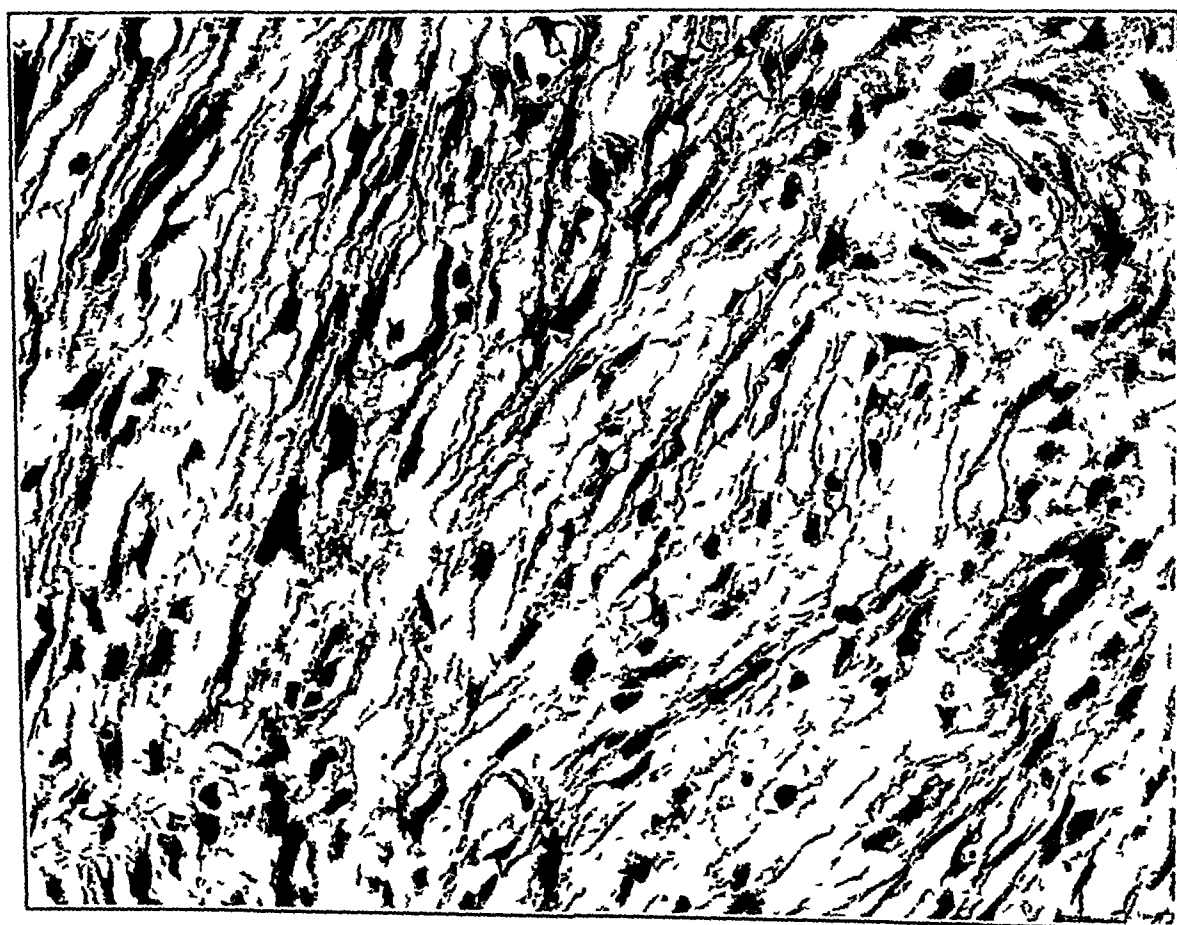


Fig 2—Abundant longitudinal cavities among the connective tissue fibrils, probably caused by extraction of a fatlike substance during the alcohol treatment of the sections (trichromic stain, $\times 450$)

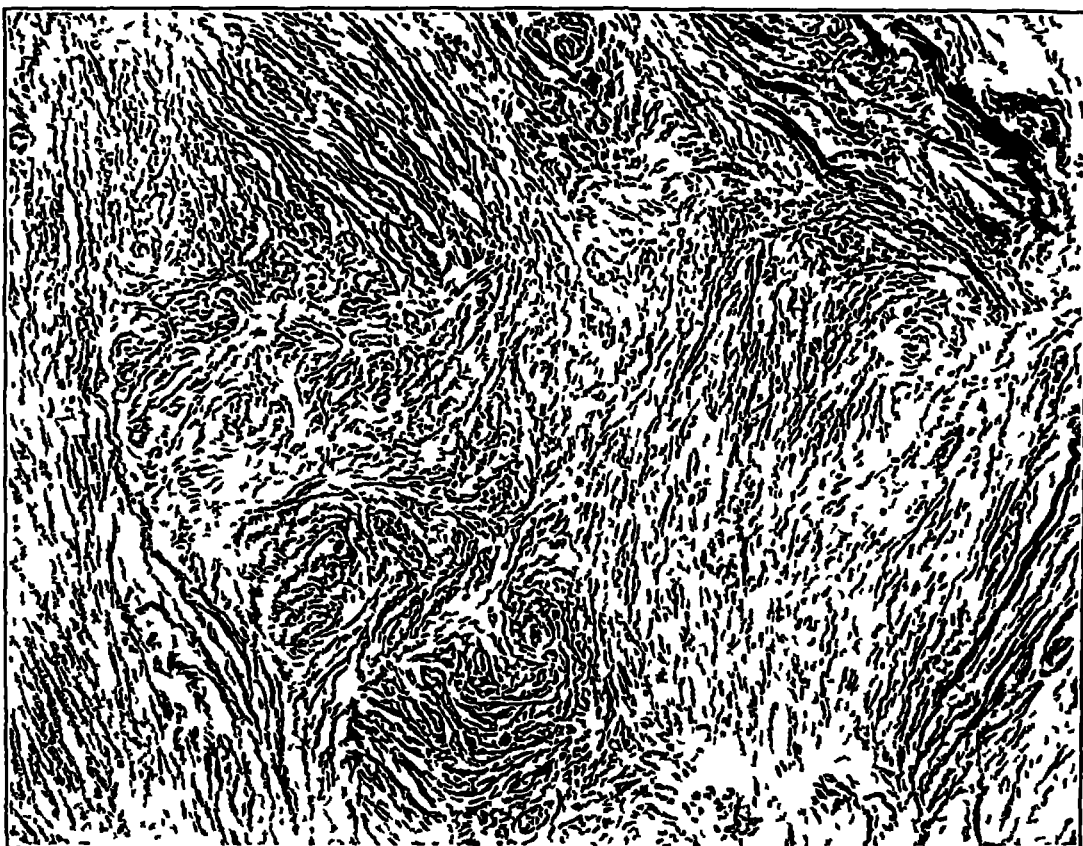


Fig 3—Condensed connective tissue arranged in irregular whorls (trichromic stain, $\times 132$)



Fig 4—Brown-red masses in the stratum reticulare cutis (sudan IV stain, $\times 37$)

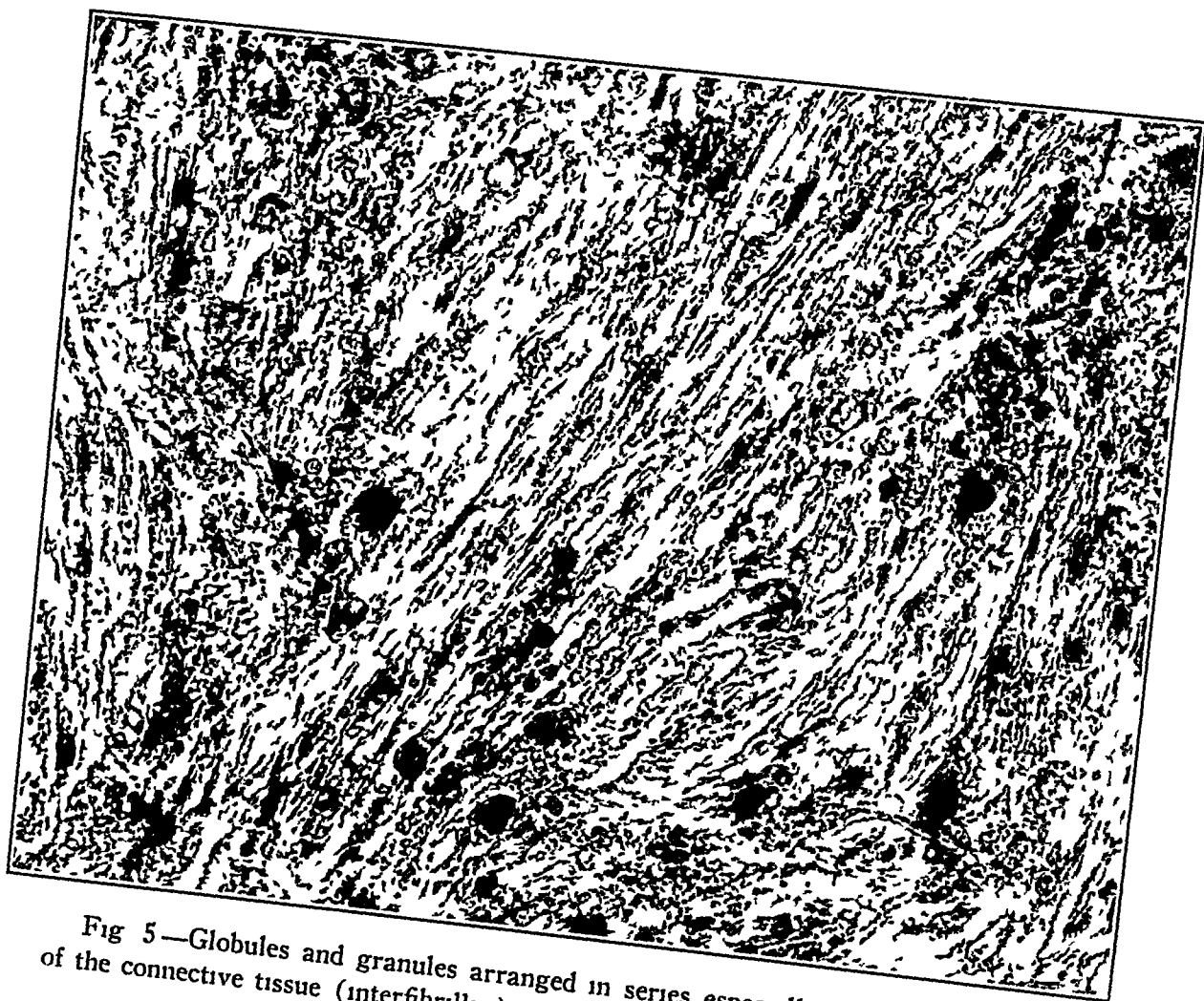


Fig 5—Globules and granules arranged in series especially between the fibrils of the connective tissue (interfibrillar) (sudan IV, $\times 450$)

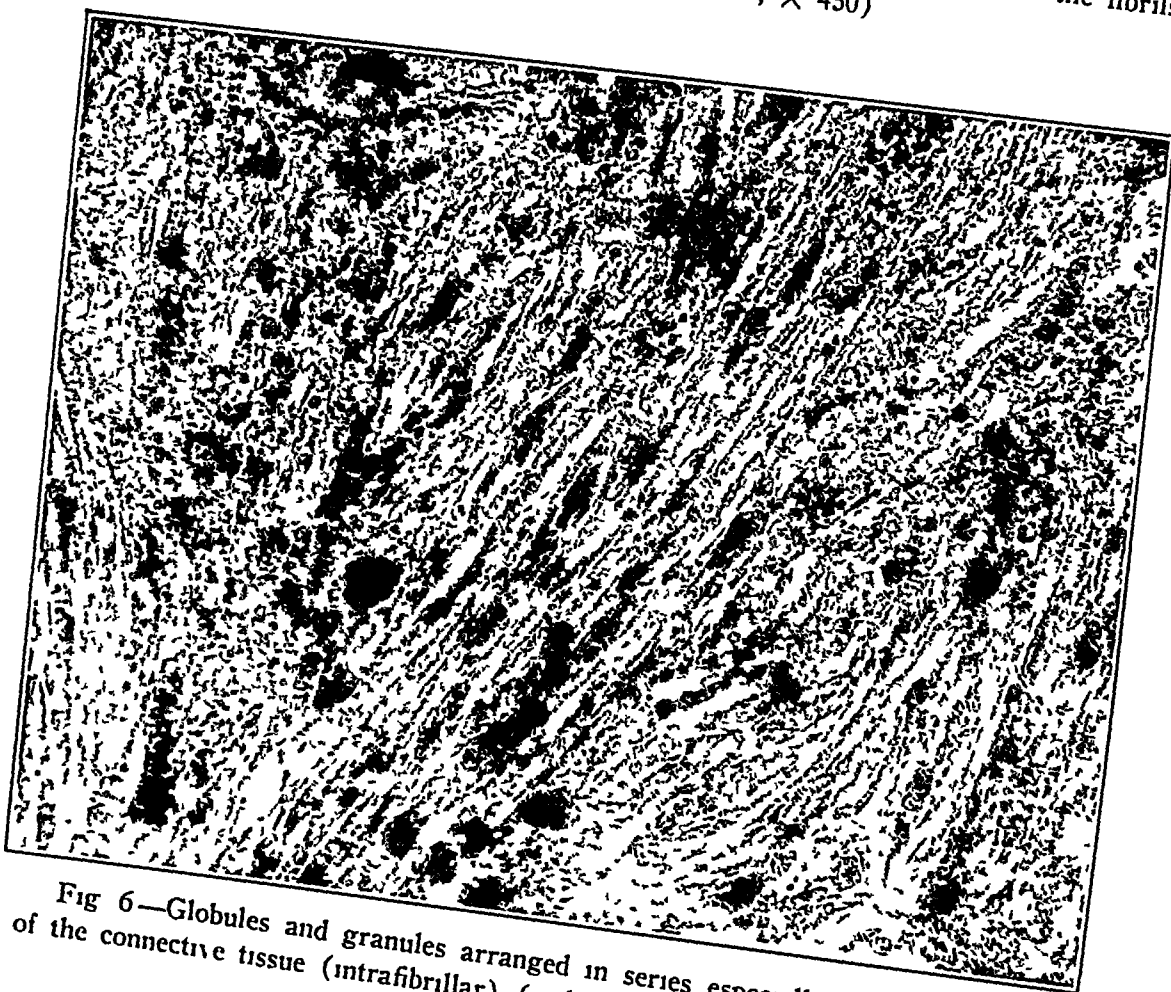


Fig 6—Globules and granules arranged in series especially within the fibrils of the connective tissue (intrafibrillar) (sudan IV, $\times 700$)

Sudan IV Stain—The stratum reticulare at low magnification became brown-red in the region of the altered cutaneous areas (fig 4) On greater microscopic magnification globules and granules appeared to be arranged in series, especially between and within the fibrils of the connective tissue (figs 5 and 6) Fat appeared rarely in the cytoplasm Foam cells could not be demonstrated anywhere This lipoid was soluble in ether and boiling hot acetone, it was largely, but not completely, soluble in cold acetone and cold or boiling absolute alcohol and insoluble in chloroform

Nile Blue Sulfate Stain—Pine-colored globules and granules were present

Smith-Dietrich Stain—The fat present was a so-called lipoid and was not neutral fat

Fischler Stain—No fatty acids or soaps were present

Crystal Violet Stain—Amyloid was not present

Von Kossa Stain—Calcium was not formed

Polarization Microscopic Examination—Double refractive bodies were not demonstrable

COMMENT

We have been dealing with 2 patients in whom after trauma (vaccination) and hematogenous infection (rheumatism), respectively, there developed one or more inflammatory nodules in the skin, exhibiting a yellowish color indicative of increased lipoid content On histologic examination, it was found that predominantly connective tissue was involved Here two different forms, or perhaps phases, must be distinguished In some parts of the skin there appeared extraordinary proliferation of connective tissue cells and condensation of the connective tissue fibrils Between these were cleftlike irregularly limited cavities without a cellular lining and, on being stained with sudan, found to be filled with lipoid In other words, fat was abundantly deposited in the form of granules and droplets in the fibrillary connective tissue In other parts the connective tissue cells seemed somewhat diminished in size as compared with the normal, the connective tissue fibrils, on the other hand, were thick and lumpy or even broken off The pathologic result of the Van Gieson and Weigert stains is a further proof that this connective tissue was diseased Considering the fact that the collagen had lost its normal affinity for the acid stains and, on the contrary, showed an avid affinity for the basic stains contained in the polychrome methylene blue stain of Unna, the condition must be considered a so-called basophilic degeneration of the collagen

A remarkable feature was the complete absence of inflammatory cells, of giant cells and, most particularly, of foam cells As regards the type of fat present, considering the absence of double refraction and the results of the lipoid solubility tests, one may be sure that it was not cholesterol fatty acid ester or free cholesterol Whereas both of these are completely soluble in hot alcohol and insoluble in boiling acetone, the lipoids in both cases which formed the basis for this report

were completely soluble in boiling acetone and only comparatively, but not completely, soluble in boiling alcohol

Thus, this lipoid dermatosis is so definitely differentiated clinically, histologically and histochemically that we feel justified in introducing it as a new disease entity with the name *imbibitio lipoidica collageni degenerati cutis*

We have still to explain why we consider the condition an imbibition and its classification as a local lipoid disease, in spite of the fact that in both cases reported there appeared a considerable increase in the level of blood cholesterol and in the second case an increase in the total lipids as well (the latter might have been present also in the first case although not manifest in the figures, because the examination was conducted after three weeks of a strictly fat-free diet) The reason for the assumption of a local secondary lipoidosis was that such a lipoid absorption did not occur until years after the appearance of the cutaneous lesions This fact was proved by the 'negative lipoid findings in tumors of three years' duration in the first case and further by the absence of lipoid in the cells and its presence only in the fibrillary connective tissue, which presented severe symptoms of degeneration From these observations, we conclude that the change in the connective tissue was the primary lesion and that lipoid imbibition occurred as a secondary process

A review of the literature shows that the disease which we have described has apparently been known for several years under other names Woringer and Kwiatkowski⁵² were the first to draw attention to the fact that the cutaneous nodules described by Unna⁵³ as "fibroma simplex," by Arning and Lewandowsky⁵⁴ as "noduli cutanei," by Schreus⁵⁵ as "dermatofibroma lenticulare" and by Michelson⁵⁶ as "nodular subepidermal fibrosis" possessed the capacity for absorbing fat Of the opinion that this fat was stored by the histiocytes of the skin, they named it "histiocytoma of the skin" Sézary and Lévy-Coblentz⁵⁷ accepted this nomenclature in an article which they published under the characteristic title "From Histiocytoma to Xanthoma," believing that a

52 Woringer, F, and Kwiatkowski, S L L'histiocytome de la peau, *Ann de dermat et syph* 3:998, 1932

53 Unna, P G The Histopathology of the Diseases of the Skin, translated by N Walker, New York, Macmillan & Co, 1896, p 836

54 Arning, E, and Lewandowsky, F Noduli cutanei, eine bisher wenig beobachtete Hautaffektion, *Arch f Dermat u Syph* 110:3, 1911

55 Schreus, H T Dermatofibroma lenticulare, *Arch f Dermat u Syph* 161:456, 1930

56 Michelson, H E Nodular Subepidermal Fibrosis, *Arch Dermat & Syph* 27:812 (May) 1933

57 Sézary, A, and Lévy-Coblentz, G De l'histiocytome au xanthome, *Bull Soc franç de dermat et syph* 40:798, 1933, Fibrome en pastille et histiocytome, *ibid* 40:1269, 1933

transition from fat-containing fibromas to xanthomas is possible Pautrier and Woringer⁵⁸ advocated the term histiocytoma for those lesions in which the infiltration with lipoids is relatively slight and the term xanthoma for those in which the cells are supercharged with lipoids, producing cells of the Chambard type Lewis and Sachs⁵⁹ claimed that the lipoidal histiocytomas were fibroxanthomas The most exhaustive work must be credited to Senear and Caro,⁶⁰ who described 25 cases, in some of which there was a definite history of injury to the skin preceding onset of the condition The lesions varied in size from 1 mm to 2 cm, were round or ovoid and varied from slightly grayish brown to deep violaceous red, some nodules showing a definitely yellowish hue and peripheral scales The consistency was of a wooden hardness Senear and Caro definitely emphasized that they were never able to demonstrate any formation of foam cells but that double refraction could be demonstrated Because the cells reabsorbed subcutaneously injected saccharated ferric oxide, they considered them to be histiocytes The authors admitted frankly, however, that the designation "histiocytoma cutis" was open to criticism because one had here to deal not with a true tumor of spontaneous origin but one associated with an inflammatory histiocytosis Senear and Caro opposed the classification of these tumors in the group of xanthoma, chiefly because no foam cells or Touton's giant cells were demonstrable

From the clinical description of the lipoid-containing nodules one might conclude that they were identical with those herein described There exists, however, a fundamental histologic difference Whereas the authors cited emphasized repeatedly that the lipoid was intracellular, we were able to demonstrate in our cases that the lipoid was exclusively interfibrillary and intrafibrillary In spite of the fact that we were able to examine four different nodules histologically and that numerous sections were thoroughly studied, we could not demonstrate any lipoid deposition in the histiocytes

On the basis of our painstaking histologic and chemical examinations we therefore claim that the fibroma-like nodular structures described by Woringer and Kwiatkowski⁵² are to be interpreted as xantheloids, whereas in our 2 cases we had to deal with a so-called imbibitio lipoidica collageni degenerati cutis

Urbach gave the name "xantheloid" to all tumors which have the capacity for storing lipoid substances in their cells We oppose design-

58 Pautrier, L. M., and Woringer, F. *L'histiocytome de la peau*, Bull Soc franç de dermat et syph 40 1659, 1933

59 Lewis, G. M., and Sachs, W. *Lipoidal Histiocytoma (Fibroxanthoma)* Report of Case, Ann Int Med 9 1746 (June) 1936

60 Senear, F. E., and Caro, M. R. *Histiocytoma Cutis*, Arch Dermat & Syph 33 209 (Feb) 1936

nations such as xanthofibroma and xanthofibrosarcoma, because they convey the false impression of a combination of fibroma with some other type of tumor

Although these xantheloids are usually characterized by so-called foam cells and giant cells, Krogus,⁶¹ Garrett⁶² and other writers have emphasized the facts that neither the xanthelasma nor the Chambard-Touton giant cells constitute constant features of these tumors and that, on the contrary, the cells of fibroma, sarcoma and granuloma may all store lipoids

The differential diagnosis must take into consideration, besides Woringer's xantheloids,⁶² also a series of other lipid-containing cutaneous nodules. The lipid granuloma described by Chester and Kugel⁶³ in generalized xanthelasmatisis may be distinguished not only clinically but also by its three types of cells, typical foam cells, exudate cells and younger connective tissue cells. Makai's⁶⁴ "lipidgranulomatosis subcutanea" consists of subcutaneous nodules in the skin of amputation stumps, which are to be considered as foreign body granuloma. They develop owing to the extrusion of fat from fat cells, due to the constant exposure of the subcutaneous fatty tissue to pressure. The result of this irritation is the aforementioned foreign body granuloma. The sharply defined hard violet-brown plaques of our cases have a certain clinical similarity to the Darier-Roussy sarcoid, certain forms of cutaneous amyloidosis and, particularly, necrobiosis lipoidica. The characteristic histologic picture of the three mentioned dermatoses permits their rapid distinction from the lipid dermatosis herein presented.

SUMMARY

This study contains a suggested classification for lipoidoses according to clinical, histologic and chemical criteria, an introduction of the concept of "imbibitio lipoidica" in the place of that of "lipoid degeneration" and a presentation of a new local lipid dermatosis, "imbibitio lipoidica collageni degenerati cutis."

61 Krogus, A. Zur Kenntnis der sogenannten Xanthosarkome der Sehnen-scheiden, *Acta chir Scandinav* **55** 363, 1923

62 Garrett, C. A. Tumors of the Xanthoma Type, *Arch Surg* **8**:890 (May) 1924

63 Chester, W., and Kugel, V. H. Lipidgranulomatosis (Type, Hand-Schuller-Christian). Report of Case, *Arch Path* **14** 595 (Nov) 1932

64 Makai, E. Lipogranulomatosis subcutanea am Amputationsstumpf (Prothesenrandknoten), *Zentralbl f Chir* **57**:590, 1930

SCLEROSING SOLUTIONS

A PHOTOGRAPHIC METHOD FOR STUDYING THEIR EFFECTS ON TISSUE

LUDWIG ISAAK, M D
NEW YORK

Experimental studies on animals with different sclerosing solutions have been carried out before. Wolf¹ studied histologic alterations following injection of solution of mercury bichloride, Meisen² reported histologic changes following the use of sodium salicylate, and Dorffel,³ changes following the injection of sugar and saline solutions. Similar experimental studies have been made by Regard,⁴ Schwarz and Ratschow⁵ and others. As a rule the blood vessels of rabbits' ears have been used, and the veins of dogs and horses have also served.

Comparative studies of different solutions applied to the aural veins and the subcutaneous tissue of rabbits were made by Schubert⁶ in 1933. He examined and compared the effectiveness of sodium morrhuate solution of 3 to 10 per cent concentration, invert sugar solution of high viscosity and high concentration, hypertonic solution of sodium chloride and alcohol from 70 to 100 per cent. All investigators based their conclusions on the clinical aspect and the histologic observations.

For the past two years the varicose veins clinic of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital has secured effective results with relative absence of side effects by the use of an invert sugar solution of high viscosity and high concen-

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University

1 Wolf, E. Die histologischen Veränderungen der Venen nach intravenösen Sublimatenspritzungen, *Med Klin* 16 800, 1920

2 Meisen, V. A Lecture on Injection Treatment of Varicose Veins and Their Sequelae (Eczema and Ulcer Cruris) Clinically and Experimentally, *Acta chir Scandinav* 60 435, 1926

3 Dorffel, J. Experimentelles und Klinisches über Krampfaderverödung, *Dermat Ztschr* 51 41, 1927

4 Regard, G. L. Le traitement des varices par les injections sclérosantes, *Rev med de la Suisse Rom* 45 102, 1925

5 Schwarz, E., and Ratschow, M. Experimentelle Untersuchungen über die künstliche Verödung von Venen, *Zentralbl f Chir* 56 1474, 1929

6 Schubert, M. Experimentelle Untersuchungen über die gefässveröden-
de Wirkung des Natrium morrhualicum im Vergleich mit den gebräuchlichsten
Zucker- und Salzlosungen, *Beitr z klin Chir* 157 55, 1933

tration⁷ The experiments to be reported were undertaken to find the reason for the results obtained in the clinic

The rabbit's ear is an excellent test object for comparative examinations The anatomic relations and the caliber of the blood vessels are about the same in every animal of the same size, with the arterial system in the center of the ear and the veins on the borders connected by communicating blood vessels and all visible when observed against a source of light Observations on the obliterative process of the blood vessels of the rabbit's ear indicated that the red blood vessels turned yellowish after obliteration, that inflamed areas became red, that insufficient obliteration or recanalization of the blood vessels caused them to appear again, while the obliterated veins and connective vessels once visible disappeared entirely Accordingly I followed these changes photographically After a series of experiments it has been found that photographs depicting clearly the course of events could be obtained by photographing the rabbits' ears against a flashlight

Because of the small caliber and capacity of the vein of the rabbit's ear, amounts of solutions have been used in relative proportion to the amount used and indicated for the treatment of varicose veins, according to the table of McPheeters⁸ In the following tabulations only those solutions used in my experiments are reported on

Solution	Sodium Morrhuate	Sugar	Quinine and Ethyl Carbamate (Quinine Urethane)	Sodium Chloride
Strength	½ to 10%	50 to 75%	2%	20%
Dose	0.5 to 5 cc	5 to 30 cc	0.5 to 2 cc	5 to 30 cc

Solution	Sodium Morrhuate	Invert Sugar of Low Viscosity*	Invert Sugar of High Viscosity†	Quinine and Ethyl Carbamate (Quinine Urethane)	Sodium Chloride Sodium Salicylate
Strength	5%	60%	80%	2%	30%
Dose	0.25 to 0.3 cc	0.5 cc	0.25 to 0.5 cc	0.15 to 0.25 cc	0.3 cc

* Invert sugar (Lilly) was used in these experiments

† Levodex (Endo) was used in these experiments

METHOD

With the technic based on my experience and on that of other authors, I injected the solutions either into the bloodless or into the blood-filled vein, imitating the procedure used in the treatment of varicose veins Subcutaneous and paravenous injections were also given Fine hypodermic needles with short points were used The ears were photographed prior to injection, a few days after the treatment and at the end of the observation period A lens opening of 22 was used with a no 21 flash bulb, and the photographs were taken on Defender brand H G S portrait film The lens was placed 18 to 20 inches (45 to 51 cm)

7 As an invert sugar of high concentration and high viscosity levodex (Endo) has been used, as an invert sugar of high concentration and low viscosity invert sugar (Lilly) was employed

8 McPheeters, H O, and Anderson, J K Injection Treatment of Varicose Veins and Hemorrhoids, Philadelphia, F A Davis Company, 1938

from the ears, which were held still by hand. The flash bulb was held behind and below the ears, so that the light showed through the ears without producing a halation on the photograph. The photographic plate is sensitive for red, therefore, red turns black in the picture (blood vessels and inflamed areas). Obliterated blood vessels become yellowish and are not visible in the photograph. Effective obliteration of the veins in a rabbit's ear is followed by infarct if blood circulation is not restored in due time.

EXPERIMENTS

The experimental data are presented in the accompanying tabulation.

Experiment 1

	After Four Days (Fig 1A)	After Seven Days	After Ten Days	After Eighteen Days (Fig 1B)
Left ear 0.25 cc sodium morrhuate injected into blood filled lateral vein	Slight inflammation	Inflammatory reaction decreasing	Almost normal	Normal
Right ear 0.5 cc invert sugar of high viscosity injected into bloodless vein and kept there for four minutes	Inflammation	Swelling and inflammation	Slight necrosis	Necrosis of lateral border of ear

Sodium morrhuate, 0.25 cc, injected in the blood-filled vein caused only a slight inflammation and was not effective enough to obliterate the vein. An invert sugar of high viscosity, 0.5 cc, injected in the bloodless vein and left there for four minutes obliterated the vein.

Experiment 2

	After Four Days	After Seven Days	After Ten Days	After Twenty One Days (Fig 2)
Left ear Subcutaneous injection of 0.5 cc sodium morrhuate. Dime sized wheal	Inflammation, beginning necrosis	Inflammation and necrosis, cartilage affected	Injection site covered with crust	Scarring still inflamed distortion of ear due to damage to cartilage
Right ear Subcutaneous injection of 0.5 cc invert sugar of high viscosity. Subcutaneous bleeding in wheal	Hematoma, ear inflamed	Superficial necrosis	Injection site covered with crust	Scarring still inflamed

Both sodium morrhuate, 0.5 cc, and invert sugar of high viscosity, 0.5 cc, injected subcutaneously caused inflammation and necrosis. The sugar solution affected the skin only, whereas the sodium morrhuate damaged the cartilage.

Experiment 3 (Same Animal)

	After Three Days	After Five Days (Fig 3A)	After Eight Days	After Ten Days	After Fifteen Days	After Twenty Four Days (Fig 3B)
Left ear 0.3 cc of a 70% solution of sodium salicylate injected into blood filled vein *	Inflammation, ear drooping	Severe inflammation	Beginning necrosis	Demarcation of necrosis	Still inflamed demarcation progressing	Infarct
Right ear 0.3 cc of a 70% solution of sodium chloride injected into blood filled vein	Inflammation	Inflammation	Slight necrosis	Demarcation	Less inflammation border covered with crusts	Infarct

* Rabbit cried during the injection, perhaps some drops of the solution entered paravenously.

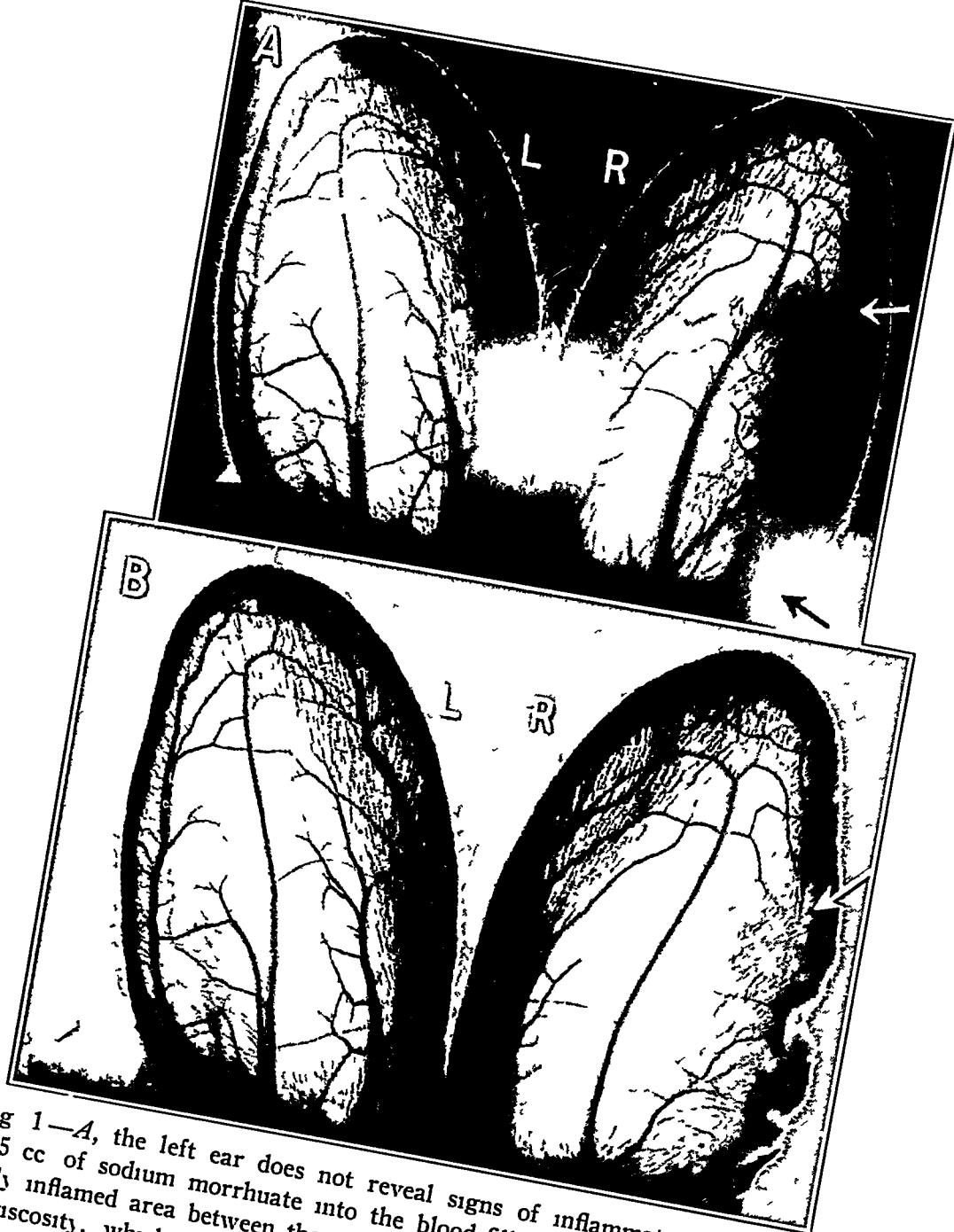


Fig 1—A, the left ear does not reveal signs of inflammation after injection of 0.25 cc of sodium morrhuate into the blood-filled vein. On the right ear the severely inflamed area between the arrows is due to 0.5 cc of an invert sugar of high viscosity, which was injected into the bloodless vein and kept there for four minutes. Halation is present because the flashlight was not held low enough. B, the left ear is normal (failure of sodium morrhuate). The right ear shows obliteration of the lateral vein below the injection site (indicated by arrow), causing infarct.

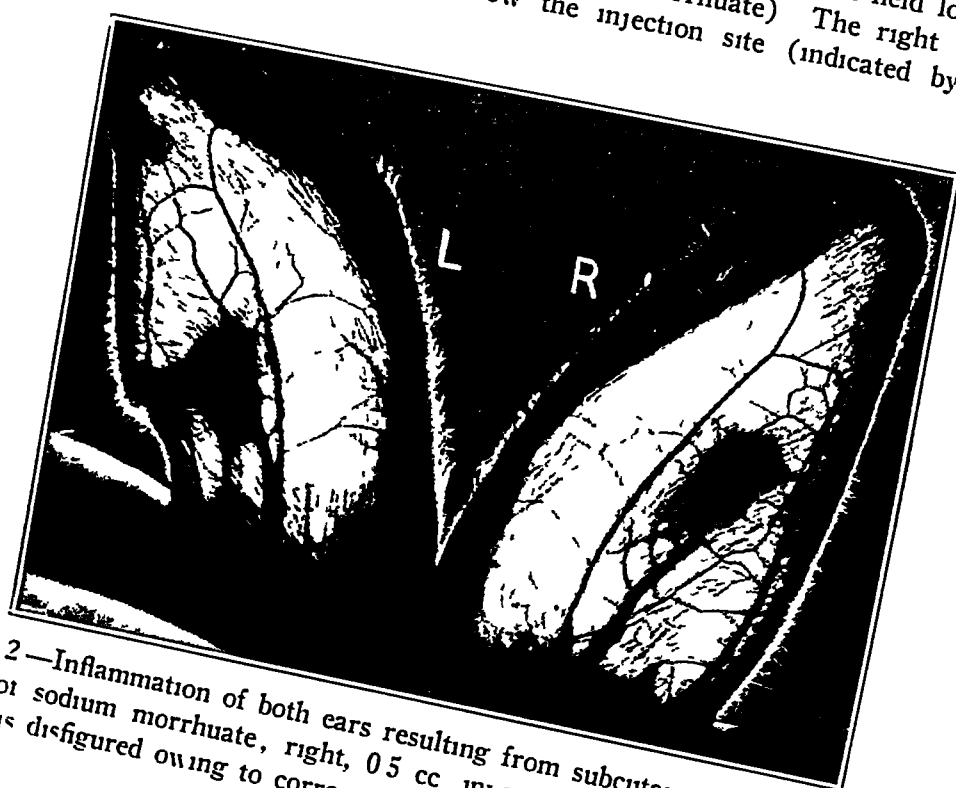


Fig 2—Inflammation of both ears resulting from subcutaneous injections. Left, 0.5 cc of sodium morrhuate; right, 0.5 cc invert sugar of high viscosity. The left ear is disfigured owing to corrosion of the cartilage.

Sodium salicylate and sodium chloride caused obliteration

Experiment 4

	After Three Days	After Five Days (Fig 4A)	After Ten Days	After Fifteen Days	After Twenty Four Days (Fig 4B)
Left ear 0.3 cc sodium morrhuate injected into blood filled vein	Inflam- mation, drooping ear	Ear swollen and inflamed	Lateral side of ear swollen and inflamed	Shrinking of border line inflam- mation still present	Infarct
Right ear 0.5 cc of a 60% solution of invert sugar of low viscosity injected into blood filled vein	No reaction				Normal

Injection of invert sugar of low viscosity, 0.5 cc of a 60 per cent solution, into a blood-filled vein was ineffective. Obliteration was caused by 0.3 cc of sodium morrhuate.

Experiment 5 (Same Animal)

	After Two Days
Right ear 0.25 cc of a 2% solution of quinine and ethyl carbamate (quinine urethane) injected into blood filled vein	No reaction

Failure resulted from use of quinine and ethyl carbamate (quinine urethane), 0.25 cc

Experiment 6

	After One Day	After Three Days	After Five Days (Fig 5A)	After Ten Days	After Nineteen Days (Fig 5B)
Left ear 0.5 cc of physiologic solution of sodium chloride injected subcutaneously, wheal	Slight inflam- mation	Reaction subsided Levodex, 0.5 cc, in- jected into blood filled vein	Inflam- mation of lateral side of ear	Slight inflam- mation, with some knots in vein	Disappear- ance of lower half of vein no inflam- mation
Right ear 0.15 cc of a 2% solution of quinine and ethyl carbamate (quinine urethane) injected into a blood filled vein	No reac- tion	Slight pinhead sized area of inflam- mation	Pea sized area of inflam- mation	Reaction subsided	

Physiologic solution of sodium chloride, 0.5 cc subcutaneously, did not affect the tissue. Quinine and ethyl carbamate (quinine urethane), 0.15 cc, injected into a blood-filled vein was a failure. An invert sugar of high viscosity, 0.5 cc, injected into a blood-filled vein obliterated the vein.

Experiment 7 (Same Animal)

	After Ten Minutes	After Two Days (Fig 6A)	After Six Days	After Fifteen Days	After Nineteen Days (Fig 6B)
Left ear 0.25 cc of a 2% solution of quinine and ethyl carbamate (quinine urethane) injected paravenously	Site of injection bleached	Extensive inflamma- tion and beginning necrosis	Beginning demarka- tion of necrosis	Dry necrosis	Necrosis of large area
Right ear 0.25 cc of invert sugar of high viscosity injected into bloodless vein and kept there for four minutes	Slight inflam- mation along vein	Inflam- mation	Inflam- mation, border of ear covered with crusts	Vein oblit- erated slight super- ficial scar ring on internal surface a little inflam- mation still visible	Still slight inflamma- tion present slight scar ring vein obliterated

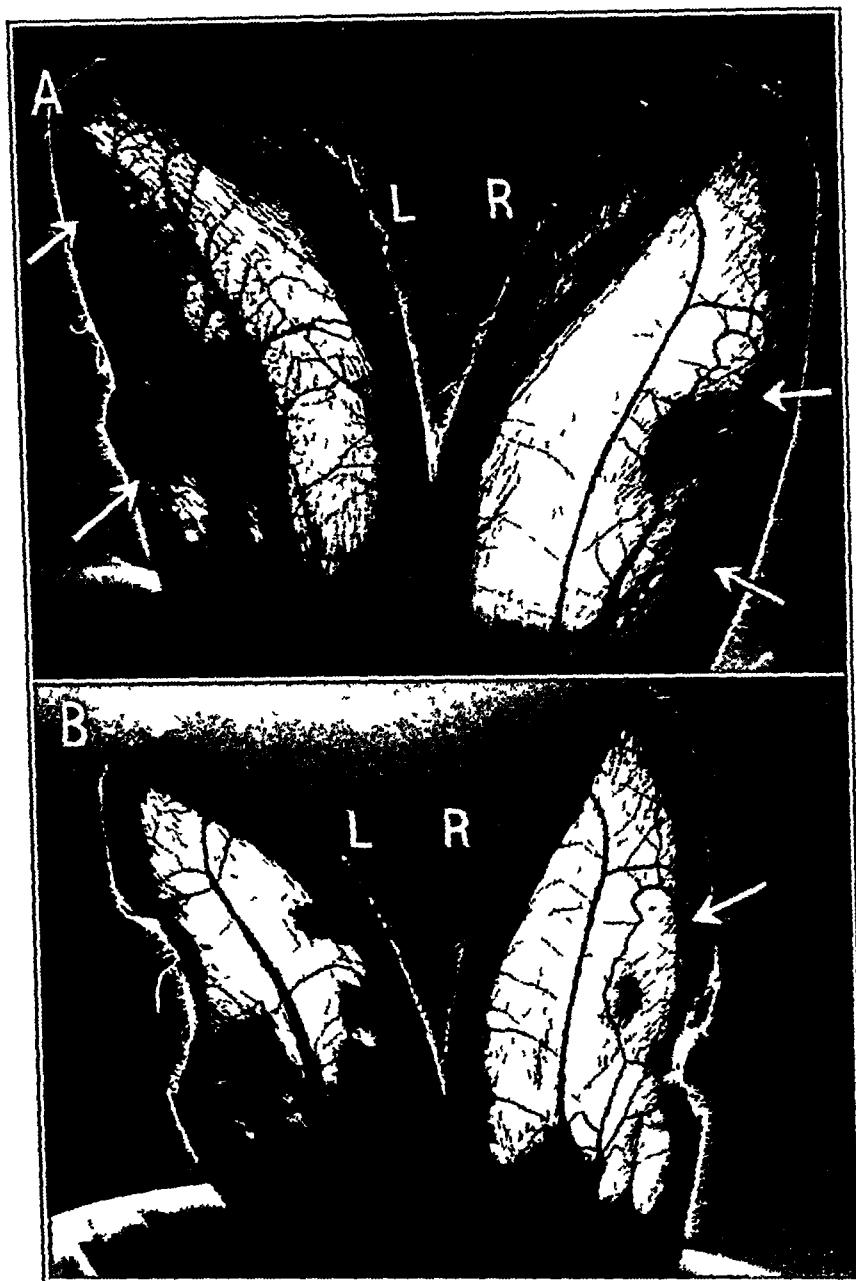


Fig 3—*A*, the intensive inflammation of the left ear results from the intravenous and probably accidental paravenous injection of 0.3 cc of sodium salicylate. The inflammation of the right ear is due to 0.3 cc of sodium chloride which was injected into the blood-filled vein. *B*, necrosis of the left ear and infarct of the right ear, with obliteration of the lateral vein below the point indicated by the arrow (fig 2). The inflammatory processes of both ears are injury marks due to the fastening of metal ear tabs by mistake and their later removal.

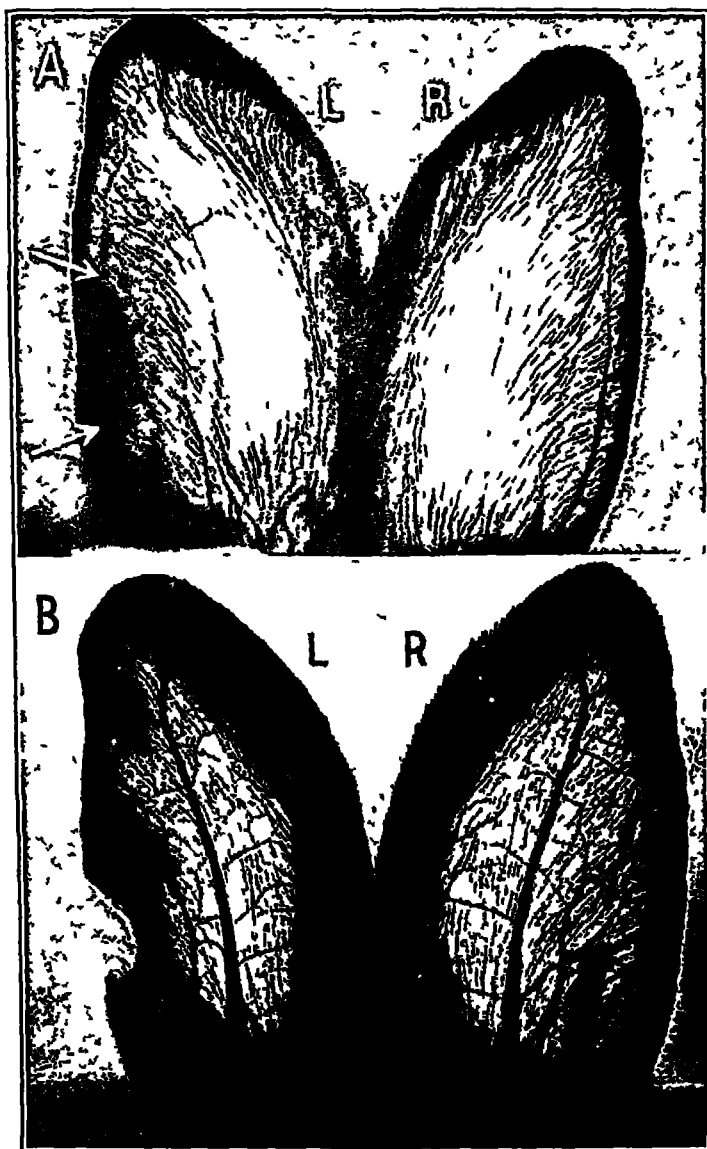


FIG 4—*A*, the lateral vein of the left ear is invisible in the inflamed tissue as a result of 0.3 cc of sodium morrhuate which was injected into the blood-filled vein. The right ear is normal after injection of 0.5 cc of a 60 per cent solution of invert sugar of low viscosity into the blood-filled vein. The picture is poor. Perhaps the flashlight was held too far from the ears. *B*, infarct of the left ear indicates effectiveness of sodium morrhuate. The normalcy of the right ear vein proves the failure of invert sugar of high concentration and low viscosity.

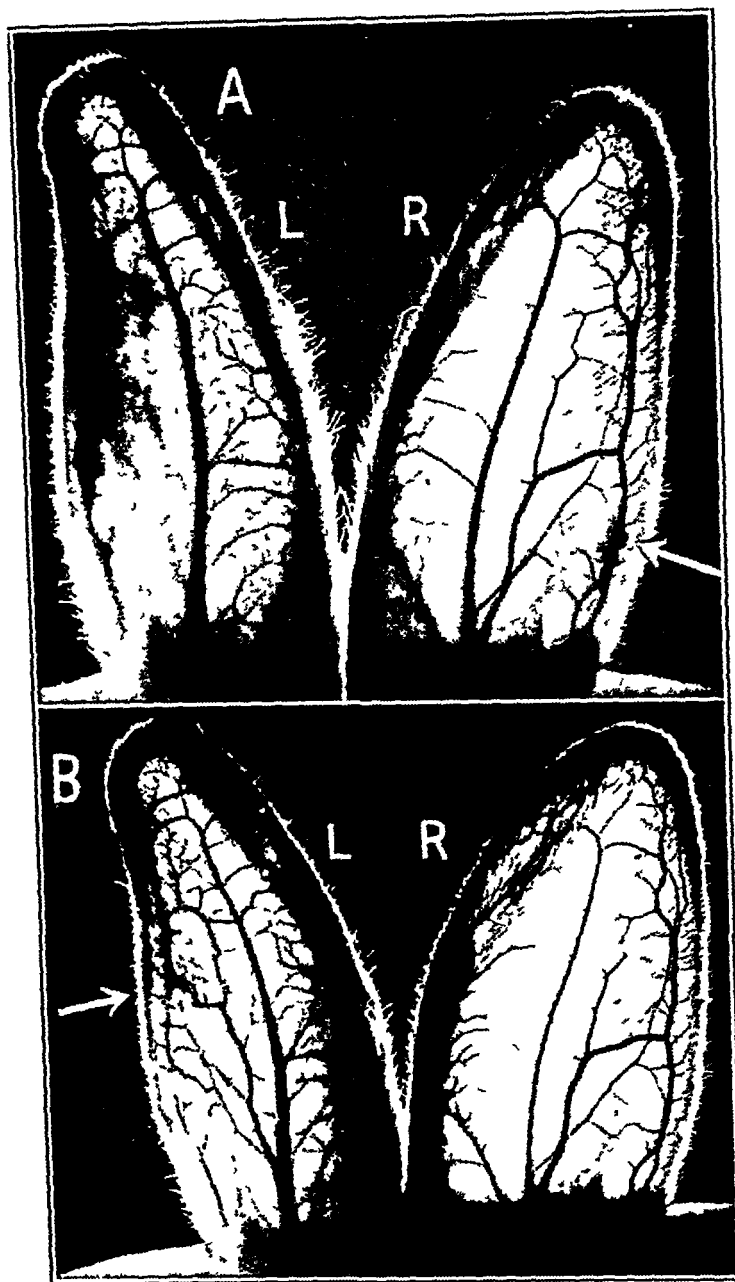


Fig 5—*A*, the left ear shows inflammation in the lateral part and haziness of the blood vessels after the injection of 0.5 cc of invert sugar of high viscosity into the blood-filled vein. On the right ear (arrow) is a pea-sized area of inflammation resulting from 0.15 cc of quinine and ethyl carbamate (quinine urethane) injected into the blood-filled vein. *B*, the obliteration of the lateral vein of the left ear below the site indicated by the arrow demonstrates the effectiveness of invert sugar of high viscosity, the normalcy of the right ear, the failure of quinine and ethyl carbamate.

Severe necrosis occurred after paravenous injection of 0.25 cc of quinine and ethyl carbamate (quinine urethane). Obliteration of vein was caused by the injection of 0.25 cc of invert sugar of high viscosity into bloodless vein.

TABLE 1—*Summary of Experiments*

Solution	Amount	Administration	Result
Sodium chloride, 80%	0.3 cc	In blood filled vein	Obliteration, infarct
Sodium salicylate, 80%	0.3 cc	In blood filled vein	Obliteration, infarct
Sodium morrhuate, 5%	0.3 cc	In blood-filled vein	Obliteration, infarct
Sodium morrhuate, 5%	0.25 cc	In blood filled vein	No obliteration
Sodium morrhuate, 5%	0.5 cc	Subcutaneously	Necrosis of skin and cartilage
Quinine and ethyl carbamate (quinine urethane), 2%	0.15 cc	In blood filled vein	No obliteration
Quinine and ethyl carbamate (quinine urethane), 2%	0.25 cc	In blood filled vein	No obliteration
Quinine and ethyl carbamate (quinine urethane), 2%	0.25 cc	Paravenously	Severe necrosis
Physiologic solution of sodium chloride	0.5 cc	Subcutaneously	No reaction
Invert sugar of low viscosity, 80%	0.5 cc	In blood filled vein	No reaction
Invert sugar of high viscosity, 80%	0.5 cc	In blood filled vein	Obliteration
Invert sugar of high viscosity, 80%	0.5 cc	In bloodless vein	Obliteration, infarct
Invert sugar of high viscosity, 80%	0.25 cc	In bloodless vein	Obliteration only
Invert sugar of high viscosity, 80%	0.5 cc	Subcutaneously	Necrosis of skin

The experiments and pictures support my clinical observations.⁹

TABLE 2—*Summary of Clinical Observations*

Solution	Results with Careful Injection	Concomitant Symptoms	Secondary Reactions	Results from Accidental Paravenous Injections
Sodium salicylate or sodium chloride	Excellent	Intensive cramp during and after injection		Intensive paraphlebitis and slough
Invert sugar solution of high concentration and low viscosity	Failure or obliteration with frequent recanalization			Burning pain of short duration
Invert sugar solution of high concentration and high viscosity, with special technic (injection into bloodless vein)	Excellent	Slight cramp of two to three minutes' duration		Burning pain of short duration
Quinine and ethyl carbamate (quinine urethane)	Good or doubtful		Angioneurotic symptoms, quinine allergy	Painful slough
Sodium morrhuate	Excellent, good or doubtful		Allergic reaction (shock, pruritus, dermatitis)	Sometimes slough

Schubert⁹ in summarizing his results, pointed out that sugar solution is the most harmless one, it never causes extensive defects, no matter where it is injected. Hypertonic solutions of sodium chloride are the most destructive, and sodium morrhuate lies between the two extremes.

⁹ Isaak, L. High Viscosity Invert Sugar. A New Sugar Solution for a More Efficient Treatment of Varicose Veins, *M. Rec.* 147:307, 1938.

COMMENT

The experiments on the aural veins of rabbits were undertaken to test the results observed in the clinic where an invert sugar of high viscosity has been used successfully in the obliterative treatment of

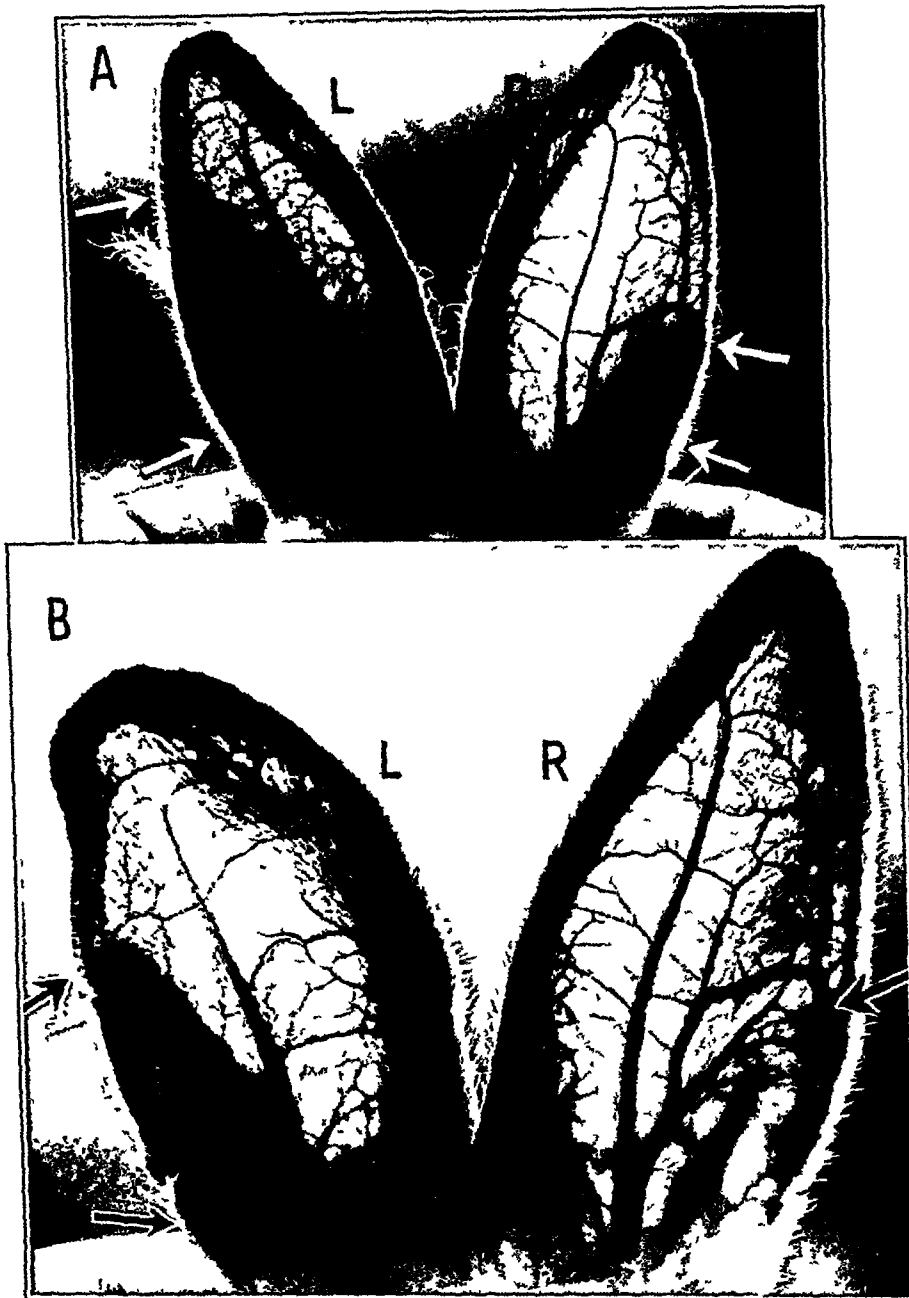


Fig 6—A, the severe inflammation of the left ear is due to the paravenous injection of 0.25 cc of quinine and ethyl carbamate (quinine urethane). The slight inflammation of the lower lateral portion of the right ear is a result of 0.25 cc of invert sugar of high viscosity injected into the bloodless vein. B, the dark area on the left ear is dry necrotic tissue, and inflammation is apparent in the demarcated zone. The right ear shows some inflammation in the lower lateral half. Below the arrow the lateral vein is invisible, showing the effectiveness of 0.25 cc of invert sugar of high viscosity injected into the bloodless vein.

varicose veins They prove that there is a difference in the obliterative effect of invert sugar solutions of high concentration and low viscosity and of invert sugar solutions of high concentration and high viscosity They justify the decision to abandon invert sugar solutions of high concentration and low viscosity in favor of a more effective solution, such as that of sodium morrhuate The experiments on animals manifest that invert sugar of high viscosity is still better and safer than sodium morrhuate in its sclerosing effect The experiments bear out clinical observations One has to admit that the technic of the administration of the invert sugar of high viscosity into a bloodless vein is more difficult than that of other solutions, and it is true that fewer patients can be treated in the relatively short clinical hours I observed, however, that fewer injections of levodex would cure the patients than of sodium morrhuate Few failures were noticed, and in spite of more prompt results the number of patients receiving treatment for varicose veins increased, perhaps owing to the effective treatment and the lack of by-effects and after-effects

The experiments on rabbits' ears differ from the treatment of varicose veins in that infarcts are often seen on the treated ear This is due to the fact that the blood vessels of the rabbit's ear present a system of end arteries and veins Every blockade of a larger area of blood vessels results in the formation of an infarct Obliteration without the formation of infarcts takes place only when the blood circulation is restored in due time

CONCLUSIONS

1 A method is presented which photographically shows vascular changes in rabbits' ears after injection of sclerosing solutions

2 The minimum amount of a solution necessary to obliterate a vein can be found easily by the rabbit experiment By multiplication of the amount obtained with a figure varying from 10 to 30 one can calculate the quantity of solution which will be effective in the treatment of varicose veins

3 The proposed macroscopic photographic method is preferable to the histologic method in examining sclerosing solutions, because it is more readily carried out, is less expensive and permits the observation of the whole obliterative process and the whole area, as compared with the small area of a histologic section

4 The experiments prove the correctness of the clinical observations that invert sugar solutions of high concentration and viscosity are more effective and less irritating than sodium morrhuate and other commonly used agents

LUPUS ERYTHEMATOSUS PROFUNDUS

REPORT OF AN EXAMPLE WITH CLINICAL RESEMBLANCE
TO DARIER-ROUSSY SARCOID

S IRGANG, M D
NEW YORK

Lupus erythematosus is a systemic disease with variable cutaneous manifestations. When the acute or chronic inflammatory reaction involves primarily the upper layers of the skin, it produces a distinctive aspect. On the other hand, when the point of attack of a chronic process is principally centered in the lower half of the cutis and in the subcutis, the resultant picture is entirely unlike that of the superficial variety, for here the clinical phenomenon simulates the sarcoid of Boeck and that of Darier and Roussy and also erythema induratum.

In the interest of better understanding, chronic lupus erythematosus should be subdivided further into three types according to the point of maximum reaction in the skin, namely, the superficial, the median and the deep. The last two types possess infiltrative qualities which produce tumor-like formations. The first type includes both the localized and the disseminate form, which are well known to all dermatologists, the second simulates, clinically, sarcoid of Boeck, and the last has a definite clinical resemblance to Darier-Roussy sarcoid and to erythema induratum.

A digest of the literature discloses a rather confusing state of affairs as regards the infiltrative forms of lupus erythematosus. Whenever a case of lupus erythematosus resembling Boeck's sarcoid, or vice versa, is presented for discussion without a report of the microscopic observations, the debate rarely terminates harmoniously. Whitehouse¹ summed up the situation when, in commenting on a debate, he aptly remarked, "this is the usual discussion one hears." Weidman² was truly confused by the term "transition sarcoid," coined by Stokes for the infiltrated type of lupus erythematosus. Since the histologic aspect of early sarcoid with its banal inflammatory response might prove misleading in differ-

From the Department of Dermatology and Syphilology, Harlem Hospital

1 Whitehouse, H. H., in discussion on Maloney, E. R. - A Case for Diagnosis (Lupus Erythematosus, Sarcoid or Erythema Perstans?), Arch. Dermat. & Syph. **31**:439 (March) 1935.

2 Weidman, F. D., in discussion on Stokes, J. H. - Transition Sarcoid. Lupus Erythematosus vs Sarcoid vs Angiolupoid, Arch. Dermat. & Syph. **32**:694 (Oct) 1935.

entiation from lupus erythematosus, this situation could not be applied to the case in question, since the eruption had been present for about six months. In the discussion that followed, Stokes agreed with Weidman that the patient had lupus erythematosus. While it might be possible to unite sarcoid and lupus erythematosus on a clinical and etiologic basis, there is no need for coining a new phrase in this instance, because the microscopic picture created by each is distinctive and entirely dissimilar in fully developed conditions. It is not possible to make a diagnosis of the infiltrated type of lupus erythematosus without recourse to the microscope. Furthermore, multiple diagnoses in the same patient frequently lead to error, yet discussers will agree to a diagnosis of lupus erythematosus and sarcoid in the same patient on clinical grounds alone.³

Brocq⁴ was probably the first to describe the deep form of lupus erythematosus. Years later Kren⁵ and Oppenheim⁶ presented typical cases of this disease before the Viennese Dermatological Society. Fordyce⁷ was one of the pioneer American dermatologists to consider the possible existence of lupus erythematosus profundus. His patient, a woman aged 20, had typical lupus erythematosus superficialis of the face, with multiple subcutaneous nodules on the face and arms. He considered the subcutaneous tumors and the lupus erythematosus superficialis to have the same causation, but since no histologic report was at hand, the discussers classified the subcutaneous nodules with sarcoids of the Darier-Roussy type.

Oliver's⁸ patient, a woman aged 35, had a superficial type of lupus erythematosus for three years, involving the scalp, face and arms. Two months prior to presentation deep-seated nodules appeared on the arms and buttocks. A biopsy was not made. In the discussion that followed the presentation, the deep-seated lesions were considered to be erythema induratum. That these nodules were lupus erythematosus profundus seems highly probable.

Caro's⁹ patient, a woman aged 35, presented three violaceous red subcutaneous tumors on the left leg. They were of rubbery consistency,

3 Van Rhee, G. Lupus Erythematosus and Sarcoid, *Arch Dermat & Syph* **13** 293 (Feb) 1926

4 Brocq, L. Sur la nature du lupus erythemateux, *Rev gén de clin et de therap* **9** 113 (Feb 23) 1895

5 Kren, O. Lupus erythematosus, *Arch f Dermat u Syph* **112** 391, 1912

6 Oppenheim, M. Lupus erythematosus profundus, *Arch f Dermat u Syph* **115** 847, 1913

7 Fordyce, J. A. Lupus Erythematosus with Nodular Lesions Suggesting Sarcoid, *Arch Dermat & Syph* **11** 852 (June) 1925

8 Oliver, E. L. Lupus Erythematosus, Sarcoid, *Arch Dermat & Syph* **12** 150 (July) 1925

9 Caro, M. Spiegler-Fendt Sarcoid, *Arch Dermat & Syph* **22** 1086 (Dec) 1930

IRGANG—LUPUS ERYTHEMATOSUS PROFUNDUS



Fig 1—Entire section, showing the whole skin involved in the inflammatory reaction

and they were not attached to the overlying skin. Histologically, the cutis and the subcutis were involved in the inflammatory reaction. The infiltrate consisted of many ill defined groups of cells, composed mainly of lymphocytes, the arrangement of which was perivascular and periglandular. In the deep part of the cutis and in the subcutis the lymphocytes were more numerous and densely packed. Spindle cells were in evidence, and they were more prominent in the deeper portions of the skin. The histologic diagnosis was Spiegler-Fendt sarcoid. This diagnosis was disputed, and the lesions were considered related to the sarcoid of Boeck or of Darier and Roussy. I believe that some of the cases of benign conditions reported under the Spiegler-Fendt classification of sarcoid, including the aforementioned case, are probably instances of lupus erythematosus profundus. The histologic report rendered by Cajo certainly favored the deep form of lupus erythematosus.

The case presented by Michelson¹⁰ with a diagnosis of subcutaneous sarcoid was in all likelihood one of lupus erythematosus profundus. A woman aged 43 presented numerous subcutaneous infiltrated plaques on the cheek, arms and hips. They had been present for one year and showed no evidence of ulceration, although atrophy appeared on involution. The infiltrate was diffuse and perivascular and was composed of lymphocytes and polymorphonuclear leukocytes. The sections showed decided "proliferation atrophy." Montgomery^{10a} could not correlate the clinical and histologic observations in this particular instance.

Pawlow and Makarjin¹¹ recounted the clinical and microscopic observations in a patient with lupus erythematosus profundus, which they discussed under the caption "On Tumorous Forms of Lupus Erythematosus." A number of violaceous red subcutaneous tumors had been present on the scalp for four months. The older lesions showed central atrophy. The hair follicles were decidedly dilated and filled with keratotic plugs. The reaction, however, was chiefly observed in the deep part of the cutis and in the subcutis. The perivascular infiltrate consisted almost entirely of lymphocytes. Despite the absence of an associated superficial type of lupus erythematosus, I believe the authors correctly classified the disease.

Without the coexistence of the superficial type, the dermatologist often ignores the diagnosis of the deep form of this disease, despite a

10 Michelson, H. E. A Case for Diagnosis (Subcutaneous Sarcoid?), *Arch Dermat & Syph* 22 530 (Sept) 1930

10a Montgomery, H., in discussion on Michelson¹⁰

11 Pawlow, S. T., and Makarjin, A. A. Zur Frage von tumorartigen Formen des Lupus erythematoses, *Dermat Ztschr* 59 111 (Aug) 1930

fairly characteristic histologic structure. A report on Stibbens' ¹² patient with so-called Darier-Roussy sarcoid is pertinent. A woman aged 33 had movable subcutaneous nodules on the arms and buttocks, some were flesh colored, while others varied from dark red to purple. A nodule excised from the arm showed the reaction located principally in the deep part of the cutis and in the subcutis. The lymphocyte, the chief cell type, appeared in large numbers. The vessels showed evidences of pan-

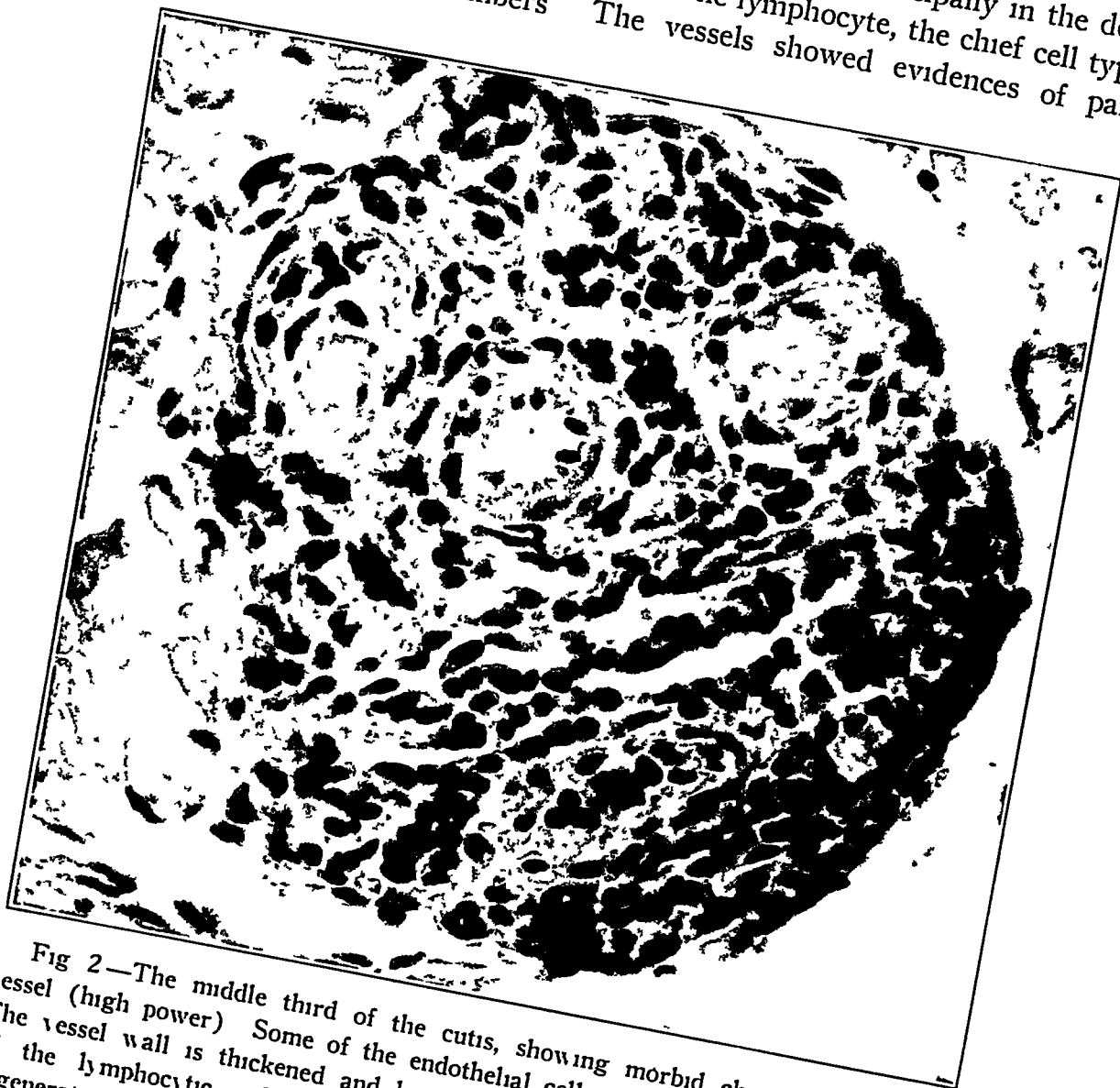


Fig 2—The middle third of the cutis, showing morbid changes in a blood vessel (high power). Some of the endothelial cells are undergoing degeneration. The vessel wall is thickened and hyperplastic. Note the perivascular character of the lymphocytic infiltrate. The stroma within this area is undergoing degeneration.

arteritis, and "proliferation atrophy" was present. Epithelioid cells were entirely lacking.

¹² Stibbens, F. H. Multiple Benign Sarcoid (Darier-Roussy Type), Arch Dermat & Syph 24 1064 (Dec) 1931



Fig 3—The entire subcutis, with the inflammatory reaction throughout. The cellular reaction is most intense in the upper third

The appearance of these deep-seated lesions in locations other than the face is disconcerting, and histologic examination is the only recourse for accurate diagnosis. If typical lesions of superficial lupus erythematosus appear practically simultaneously with subcutaneous nodules, it is more than likely that the etiologic factor is the same for both, and there is no necessity for multiple diagnoses in most instances. Comel¹³ was

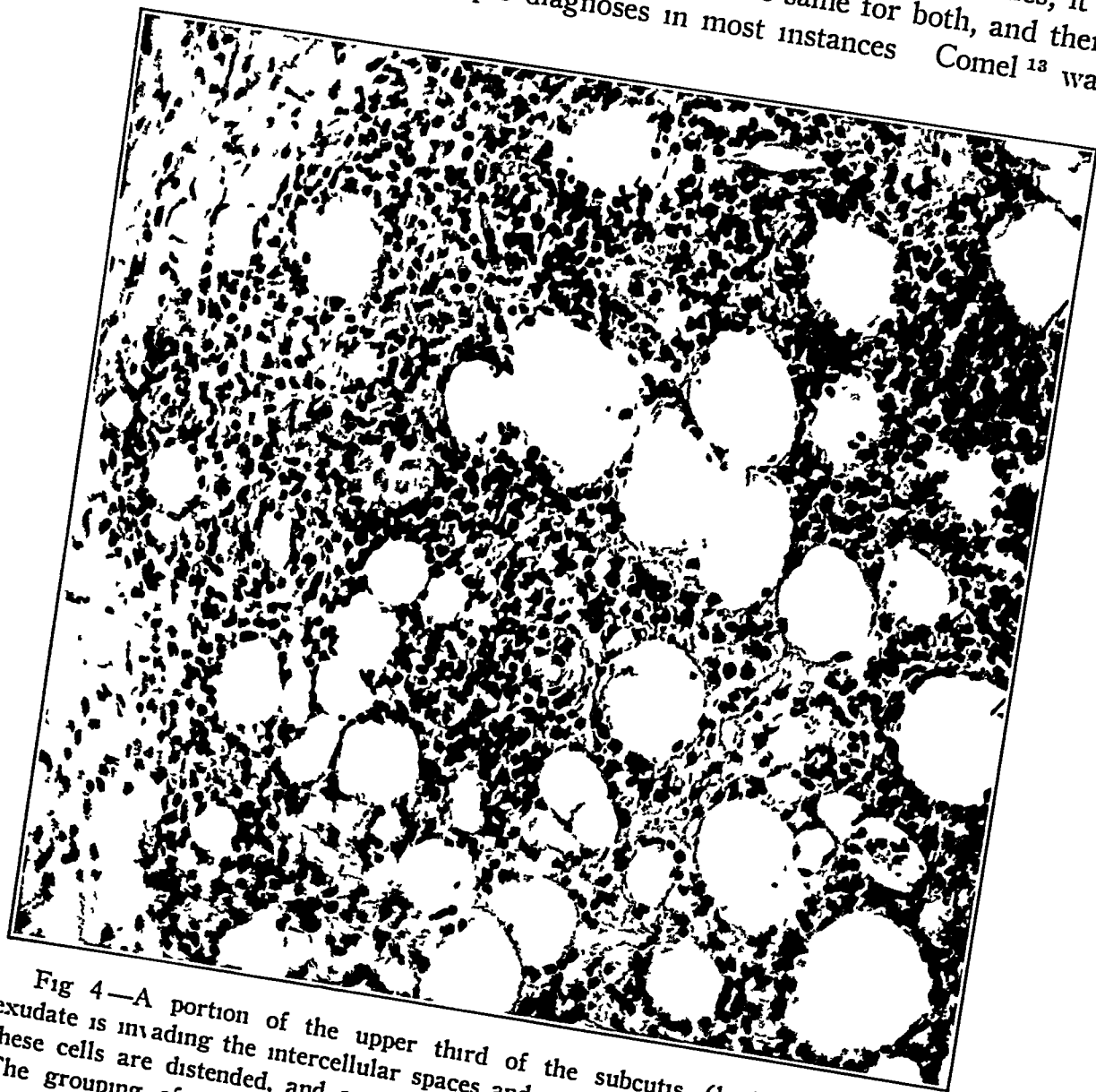


Fig 4—A portion of the upper third of the subcutis (high power). The exudate is invading the intercellular spaces and penetrating the fat cells. Some of these cells are distended, and an occasional cell wall shows evidence of rupture. The grouping of a few histiocytes at the left suggests tubercle formation, in no other part of the entire section is this feature encountered.

probably deceived by the presence of infiltrations on the lower extremities when he made a diagnosis of lupus erythematosus tumidus and

¹³ Comel, M. Lupus eritematoso tumido associato ad eritema indurato Bazin, contributo al quesito delle microbidi cutanee, *Gir ital di dermat e sif* 73:1812 (Dec) 1932

erythema induratum for the same patient, despite the similarity of the histologic structure of the lesions on the face and on the legs. These findings apparently surprised the author, who was unable to find a tuberculoid architecture in either section. Comel's patient, a woman aged 31, had had a tuberculous infection of the cervical lymph nodes for many years. Five years prior to observation small red nodules appeared on the face and on the dorsa of both hands. Two years previously irregular, deep-seated infiltrated plaques developed on the legs. The plaques were dark red to violaceous, and there was a tendency for all lesions to undergo remission and exacerbation, regardless of treatment. Examination revealed scars from a healed tuberculous infection of the cervical lymph glands and an active tuberculous process involving the submaxillary lymph glands. Comel is the authority for the statement that follicular hyperkeratosis is demonstrable only microscopically in patients with lupus erythematosus profundus and that resolution may occur with or without scar formation. He also stated that the microscope reveals edema, congestion and foci of lymphocytic infiltration.

Traub's¹⁴ patient undoubtedly had lupus erythematosus profundus, yet, despite suggestive microscopic evidence, there was no unanimous agreement among the physicians at the presentation. Fraser stated the belief that the eruption was sarcoid, although he stressed the fact that some parts of the section suggested lupus erythematosus.

Chargin and Wolf¹⁵ presented a case with a diagnosis of lupus erythematosus of the face and sarcoid of the arm. In addition to the typical superficial type of lupus erythematosus of the face, subcutaneous nodules were present. These lumpy lesions were similar to those on the arm. In the discussion the nodules on the face and arm were considered to be sarcoid either of the Boeck or of the Spiegler-Fendt type. Later a microscopic examination of sections of nodules from both localities showed identical histologic structures, and the condition was classified by several pathologists as the deep form of lupus erythematosus.

Lupus erythematosus profundus is little recognized as a definite clinical entity, and since there is lack of unanimous agreement among experienced pathologists¹⁶ as to the actual existence of this variant of lupus erythematosus, it was considered opportune to report the following case.

14 Traub, E. F. A Case for Diagnosis (Sarcoid? Lupus Erythematosus Profundus?), *Arch Dermat & Syph* **34** 538 (Sept) 1936.

15 Chargin, L., and Wolf, C. Lupus Erythematosus of the Face and Boeck's Sarcoid of the Arms, *Arch Dermat & Syph* **36** 458 (Aug) 1937.

16 Satenstein, D. L., in discussion on Chargin, L., and Wolf, C. Lupus Erythematosus of the Face and Boeck's Sarcoid of the Arms, *Arch Dermat & Syph* **40** 499 (Sept) 1939.

REPORT OF CASE

A white married woman aged 23, a native of Puerto Rico, was first seen on Jan 11, 1939. Since migrating to the United States eight years previously, she had been a resident of New York. Both her uncle and aunt had died from pulmonary tuberculosis in Puerto Rico six years and two years before, respectively. She had measles and mumps during childhood but recovered from these uneventfully.

The patient had been in apparent good health until 1936. At this time, while she was visiting her native land, large masses appeared on both sides of the neck. These superficial, painless tumors, apparently tuberculous lymphadenitis, resisted varied types of treatment but subsided gradually two years later, only to recur in milder form within six months. On admission to the clinic her symptoms were purely objective. She complained of a small mass on the back and an eruption on the face, which had been present for six months and four months, respectively. On the right cheek were four closely aggregated red superficial edematous slightly scaly lesions, varying in size from that of a pinhead to that of a split pea. A single split pea-sized lesion was present on the left cheek. A single flesh-colored well defined smooth subcutaneous flat plaque, about the size of a 50 cent piece, was observed on the upper part of the left side of the back near the shoulder. It was firm and elastic, and its elevation above the surface was barely noticeable. The skin over this mass appeared normal, there were no scales, and dilated follicular orifices were not noted. The tumor was not attached to the skin, and it was freely movable over the deep tissues. No lesions were noted on the buccal mucosa. The anterior cervical lymph glands were slightly enlarged. They were symmetric, discrete, painless, flesh colored and freely movable. The presumptive clinical diagnoses were lupus erythematosus of the face, Darier-Roussy sarcoid of the back and tuberculous lymphadenitis. In addition to the conditions noted, there was a mild hypotension, the systolic blood pressure was 104 and the diastolic 76, otherwise the results of physical examination were normal.

A biopsy was made of the lesion of the back on January 12. An intracutaneous injection of 0.1 cc of old tuberculin in dilution of 1:100,000 produced a strongly positive reaction, which persisted for about six weeks. The blood Wassermann reaction was reported as negative. The results of a urine examination were likewise negative, and a blood count gave normal results except that there were 44 per cent lymphocytes. A roentgenogram of the lung showed no abnormalities.

The facial lesions showed evidences of resolution four days after the tuberculin test and before the commencement of therapy with a gold compound, which was instituted on February 7. Eight intravenous injections of gold sodium thiosulfate were administered at weekly intervals, the initial dose was 25 mg, and the others were 50 mg except the last, which was reduced to 10 mg because of a beginning palmar keratosis. A generalized gold dermatitis appeared four days after the last treatment, that is, on April 4. It was a symmetric, intensely pruritic erythematopapular eruption. This complication resolved rather slowly with sodium thiosulfate therapy, and during the process of involution the dermatitis assumed a pityriasis-rosea-like appearance. An examination of the blood performed on May 10 showed slight secondary anemia and mild leukopenia (4,600 leukocytes per cubic millimeter), with a normal white cell differential count. On May 23 the lupus erythematosus of the face was not in evidence. The gold dermatitis having likewise completely disappeared, the patient was given weekly intramuscular

injections of bismuth subsalicylate, the initial dose was 1 cc, but later the dose was increased to 15 cc of the suspension. On July 7, or five months after the institution of aurotherapy, the subcutaneous tumor of the back and the palpable cervical lymph glands had completely disappeared. Healing of the former lesion resulted in slight atrophy. During treatment with both gold and bismuth preparations, the patient received intracutaneous injections of old tuberculin at intervals of three to four weeks. Dilutions were increased rapidly to determine the degree of sensitivity. Hyperergy to tuberculoprotein was present, since a positive reaction resulted from an injection of 0.1 cc of a 1 to 1,000,000,000,000,000 dilution.

The inflammation involved the entire skin. The stratum corneum appeared normal except in localities where it effectively plugged an occasional dilated follicular or sweat duct orifice. These localized hyperkeratoses were difficult to detect and were seen only after a number of sections were examined. Parakeratosis was absent. The epidermis was narrowed for the most part. Epidermal atrophy involved chiefly the suprapapillary rete, a few normal rete pegs were seen, but in the majority of instances they were either decidedly diminished in size or completely effaced. Areas of vacuolation were noted throughout the various layers of the epidermis. Liquefaction necrosis of the basal layer was not in evidence. The keratohyaline layer was entirely lacking in small isolated parts of the section, but in the main it was represented by a single row of cells, a number of which were in the process of vacuolar degeneration.

Edema was noticeable everywhere in the cutis and subcutis. It was both interstitial and parenchymatous. In the upper fourth of the cutis the edema was diffuse, while in the deeper portions of this area it was limited, surrounding and permeating the zones of infiltration. The collagenous fibers were widely separated and distended by the serous exudate. In the subcutis fibrinous exudate was widespread and intense. It not only separated the fat cells but also penetrated the wall of an occasional cell, with resultant distention and even rupture.

The lymph vessels of the papillary and subpapillary zones were greatly distended, in contrast to the capillaries, which were only slightly expanded. In the subcutis, however, ectasia of the latter vessels was much greater.

The compact cellular infiltration, periglandular and perivascular, was particularly intense in the lower half of the cutis and throughout the subcutis. It was well defined in the cutis but diffuse in the subcutaneous tissues. The infiltrate was composed mainly of small lymphocytes. Small to moderate numbers of histiocytes and plasma cells were likewise observed. In some foci of the lower part of the cutis, this compactness of the infiltrate was lost because of the edema within these areas, the appendages within these zones were invaded and almost completely destroyed. Within the limits of the infiltrate the collagenous fibers were in a state of degeneration. Fragmentation was especially noticeable in zones where the edema was most intense. Necrosis was absent. A decided connective tissue reaction enveloped a single nodule of infiltrate in an outlying area in the lower part of the cutis. A single blood vessel in the midcutis and another in the lower third of this area showed abnormal changes. Some of the endothelial cells were either in a state of degeneration or were completely destroyed. The vessel walls were thickened and hyperplastic. Special staining failed to show acid-fast bacilli.

COMMENT

My observations coincide with those of Comel,¹⁸ who stated that plugging of the dilated orifices of the dermal appendages is evident only microscopically in the deep infiltrated variety of lupus erythema-

tosis Involvement of the subcutis in lupus erythematosus is admittedly rare The decided edema and the cellular invasion account for the presence of the deep-seated tumors, which may be flesh colored, reddish or violaceous, depending on the degree of capillary reaction

The fact that complete resolution resulted during gold, bismuth and tuberculin therapy favors the diagnosis as presented My patient unquestionably had a tuberculous infection, which was probably contracted during adolescence The cervical adenitis more than likely resulted from activity of the tubercle bacillus, and the hyperergy to tuberculo-protein is significant A positive reaction to a dilution of 1 to 1,000,000,000,000,000 is rare in patients with lupus erythematosus The fact that the superficial facial lesions showed signs of resolution four days after the first intracutaneous injection of tuberculin favors the hypothesis of a tuberculous cause in this instance

There is no unanimity of opinion regarding the cause of lupus erythematosus Jadassohn,¹⁷ Goeckerman,¹⁸ Keil,¹⁹ Macleod²⁰ have stated that they do not believe that the incidence of tuberculosis with lupus erythematosus is any greater than with other dermatoses and that they doubt that the tubercle bacillus is a causative factor in the production of this disease On the other hand, Bloch and Fuchs²¹ were capable of inducing active tuberculosis in guinea pigs by injection of emulsified tissue from areas of lupus erythematosus Cannon and Ornstein²² confirmed these observations in 5 of 23 instances They²³ also observed that subjects with lupus erythematosus were hypersensitive to tuberculin, and this feature was especially great in those who reacted favorably to tuberculin therapy Highman, Stokes and Pollitzer²⁴ considered tuberculosis a factor in the causation of this disease

It is not within the scope of this paper to discuss in detail the pros and cons regarding the relation between tuberculous infection and lupus

17 Jadassohn, J Lupus Erythematosus, in Mráček, F Handbuch der Hautkrankheiten, Vienna, A Holder, 1904, vol 3, p 298

18 Goeckerman, W H Is Lupus Erythematosus Discoides Chronicus Due to Tuberculosis? Arch Dermat & Syph 3:788 (June) 1921

19 Keil, H Relationship Between Lupus Erythematosus and Tuberculosis Critical Review Based on Observations at Necropsy, Arch Dermat & Syph 28: 765 (Dec) 1933

20 Macleod, J M H Lupus Erythematosus Some Observations on Its Etiology, Arch Dermat & Syph 9:1 (Jan) 1924

21 Bloch, B, and Fuchs, H Ueber die Beziehungen des chronischen Lupus erythematosus zur Tuberkulose, Arch f Dermat u Syph 116 722, 1913

22 Cannon, A B, and Ornstein, G C The Tubercle Bacillus as an Etiologic Factor in Lupus Erythematosus, Arch Dermat & Syph 12:691 (Nov) 1925

23 Cannon, A B, and Ornstein, G C Lupus Erythematosus Treatment with Tuberculin, Arch Dermat & Syph 16:8 (July) 1927

24 Highman, W J, Stokes, J H, and Pollitzer, S, in discussion on Macleod²⁰

erythematosus Suffice it to say that in the case presented there was a tuberculous infection which was considered the inciting factor in the production of the cutaneous lesions

SUMMARY

Chronic lupus erythematosus should be subdivided further into three types (a) superficial, (b) median and (c) deep The latter two are definite clinical entities

Heretofore, lesions of lupus erythematosus profundus have been mistaken for Darier-Roussy sarcoid, Spiegler-Fendt sarcoid and erythema induratum

Lupus erythematosus profundus should be suspected whenever deep-seated tumor-like lesions are associated with the superficial form A definite diagnosis can be made only by histologic examination, the microscopic picture is fairly characteristic Keratotic plugging of the follicular and sweat duct orifices can be observed only microscopically, but serial sections may be necessary to show it

A case of lupus erythematosus profundus is described Hyperergy to tuberculin was demonstrated The lesion resolved during treatment with gold and bismuth preparations and with tuberculin The tubercle bacillus was probably the inciting factor

160 Riverside Drive

LXXXIX—A HISTOCHEMICAL STUDY OF NEURODERMATITIS

PRELIMINARY REPORT. MICROINCINERATION AND SPECTROGRAPHIC ANALYSIS

M F ENGMAN, M D
AND
ROSS C MACCARDLE, PH D
ST LOUIS

Chronic disseminated neurodermatitis is generally admitted by most dermatologic writers to be a definite clinical entity. The cause is unknown. It is labeled by some "atopic dermatitis," implying that the disease is allergic in nature. However, the mechanism of the production of this disease is still unknown, even if an allergic causation is assumed, since allergy itself is not entirely understood. From a therapeutic standpoint, neurodermatitis is peculiarly resistant even to an allergic regimen that usually produces results in such allergic diseases as hay fever and asthma. It seemed to us, therefore, that an entirely different approach to the study of this disease might be indicated.

Little is known about the mineral content of the skin, either in health or in disease. Electrolytes certainly play a part in the phenomena of osmosis and of surface tension. These and other powerful interacting physical forces probably enter into the production of the various phases of inflammation. The permeability of the capillaries of the skin and of the epithelial cell membrane itself may be greatly influenced by the quality and quantity of the minerals in the cell and in its environment. A study of the mineral content of the skin was therefore undertaken to determine if possible whether skin in patients with neurodermatitis differed in this respect from normal skin or from that of patients with other chronic inflammatory cutaneous diseases.

METHOD

Specimens of healthy and of diseased human skin were studied by microincineration, according to the procedure of Scott, and by a method of spectrographic analysis, described by McMillen and Scott in 1937 and since improved by Scott. By a judicious blending of the study of ashed sections of a tissue with that of its spectrograms, one can obtain a qualitative and relatively accurate quantitative estimate of its minerals in their topographic arrangement.

Studies, observations and reports from the Department of Dermatology of the Barnard Free Skin and Cancer Hospital and the Anatomical Laboratory of Washington University School of Medicine

Since there are no published reports dealing with normal human skin studied in this way, we first undertook to establish a normal base line estimate of the minerals by a study of 63 biopsy specimens of skin taken from normal persons varying in age from a few weeks to 91 years. Using the same technical procedure, we studied 24 cases of disseminated neurodermatitis. Biopsy specimens from chronically inflamed and from unaffected skin of patients with neurodermatitis were obtained. As a further control, the skin of patients with several other inflammatory cutaneous diseases was similarly studied.

Half of each specimen was prepared for microincineration, while the other half was dissolved in triply distilled nitric acid for spectrographic analysis. Spectrums of skin of patients with neurodermatitis and of normal skin of patients of comparable ages were photographed on the same plate, and all plates were developed under as nearly identical conditions as possible. The relative intensities of the lines of radiation of some of the specimens were measured microphotometrically by Mr O J Baltzer, of the physics department of Washington University.

MICROINCINERATION

In normal human skin of patients in the age group under consideration (3 years to 35) the epidermis contains a relatively large amount of the white ash of calcium and magnesium. The ashed residue of these elements in the epidermis is usually condensed around the nuclear membranes, although in the basal cells the whole cytoplasm is loaded with it. Most of the iron is contained in the cytoplasm. Few if any of the epidermal cells (of skin at this age) lack the white ash of calcium and magnesium, although the outermost cells of the spinous layer are often devoid of the residue of iron.

The epidermal cells of the skin of patients with neurodermatitis contain little of the white ash of calcium and magnesium. In active lesions even the basal cells have lost their white ash. The basal cells of unaffected skin of patients with neurodermatitis retain the white ash in amounts which appear to be normal, while the spinous cells immediately distal to them leave little of this ash after incineration. The residue of iron is located mostly in the nuclei of the spinous cells and in conspicuously larger amounts than in normal nuclei.

In other diseases, such as lichen planus and contact dermatitis, the epidermis is heavily laden with the white ash of calcium and magnesium. In those cases in which an increase of iron is noticeable, the iron oxide is found in the cytoplasm rather than in the nuclei, as in neurodermatitis. We have studied lichen planus, chronic dermatitis, contact dermatitis, senile dermatitis, exfoliative dermatitis, xeroderma pigmentosum, psoriasis and pemphigus. In all these diseases there is a decided increase in the amount of white ash of calcium and magnesium in the epidermis, but only in exfoliative dermatitis and in psoriasis is there a consistent increase in the residue of iron.

SPECTROGRAPHIC ANALYSIS

The microphotometric measurements of the relative intensities of the lines of radiation on the spectrograms of the specimens of skin studied show that the lines for calcium and zinc are of approximately the same intensity in the skin of patients with neurodermatitis and in normal and pathologic control specimens. Those for copper appear in general to be slightly less intense in the skin of patients with neurodermatitis than in either group of control specimens, but in several cases are somewhat more intense. The iron and phosphorus lines are distinctly more intense in the control specimens.

The greatest difference is in the magnesium lines. These are uniformly of less intensity in specimens of both diseased and unaffected skin of patients with neurodermatitis. There is great reduction in the magnesium content of the entire skin of patients with neurodermatitis.

SUMMARY

We wish in this preliminary report to call attention to the consistent variation in mineral content and topographic distribution peculiar to the entire skin of patients with neurodermatitis, as compared with skin both from normal subjects and from patients with a variety of other cutaneous diseases. This variation is so great in the case of magnesium that we believe there is a magnesium deficiency in the skin of patients with disseminated neurodermatitis.

THE SKIN AND CANCER UNIT OF THE NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL, COLUMBIA UNIVERSITY

A HISTORICAL REVIEW

PAUL E BECHET, M D

NEW YORK

The signing on Aug 30, 1934 of articles of agreement and affiliation between the New York Post-Graduate Medical School and Hospital, Columbia University, and the Stuyvesant Square Hospital (formerly the New York Skin and Cancer Hospital) marked an event of importance in American dermatology. The merger was a logical one, as the New York Post-Graduate Medical School and Hospital, one of the oldest graduate schools in the country, and the New York Skin and Cancer Hospital, since its inception the largest dermatologic clinic in America, frequently indulged in the interchange of clinicians and teachers even in their early years. As early as 1885 Dr George Henry Fox held classes at the New York Post-Graduate Medical School and Hospital for several years before receiving an appointment as professor; and during that time he was an attending physician at the New York Skin and Cancer Hospital and was teaching at the College of Physicians and Surgeons. Others, like Drs George T Elliot, George T Jackson, A Schuyler Clark and Henry H Whitehouse, also served both institutions at the same time. There never existed between the two anything but the best of relations, it could not well be otherwise, as their aims were somewhat different. The New York Post-Graduate Medical School and Hospital naturally placed its teaching first, while the New York Skin and Cancer Hospital devoted most of its time to clinical work. Both institutions were organized the same year, 1882.

THE STUYVESANT SQUARE HOSPITAL (FORMERLY THE NEW YORK SKIN AND CANCER HOSPITAL)

On April 8, 1882, the first institution in America devoted entirely to the care of cutaneous diseases and cancer first saw the light of day. On that memorable occasion a number of distinguished laymen, under the leadership of Dr L Duncan Bulkley, gathered in a lawyer's office and associated themselves to form a society with the following objects in view (1) the treatment of diseases of the skin and cancer by all

known medical and surgical methods, (2) the study of the etiology and pathology of cancer, (3) the study of cancer with a view to its medical treatment, and (4) the reception and care of patients with chronic cancer

This society was to be known as the New York Skin and Cancer Hospital. The certificate of incorporation was filed on Nov 11, 1882, and on Jan 1, 1883, a small private house, at 243 East Thirty-Fourth Street, was purchased for use as a dispensary and hospital for cutaneous diseases and cancer. The lower floor of this building was occupied on January 11 as a dispensary. On February 24 a small back room on the first floor was opened as a ward, with five beds. The first ward patient was admitted on February 26. The upper floors were used for hospital purposes beginning June 2, and on that date twenty-nine beds were installed.

In that first year 774 patients were treated, and in that number were included 49 with cancer. The expense for the first year, ending Sept 30, 1883, amounted to \$13,285.23. The receipts topped this by the large sum of \$41.38. Despite this strenuous financial launching, the hospital in its third year owned properties estimated at \$80,000, on its fiftieth anniversary in 1932 it had treated approximately 468,189 sufferers from cutaneous disease and cancer, and for the last five years of its existence it had treated a yearly average of 27,847 patients. By 1907, its twenty-fifth year of service, the hospital had treated 62,652 persons, who had made 281,883 visits. In the wards 7,000 patients had spent 311,309 hospital days. These figures are quoted, not in a spirit of vainglory, but simply to convey an idea of the vast amount of clinical work done.

An outstanding member of the group which founded the hospital and the one most responsible for its existence was Dr. L. Duncan Bulkley, as it was he who conceived the original idea. Dr. Bulkley was born in 1845. His father, Henry Daggett Bulkley, gave the first lectures on dermatology in America, at the old Broom Street Infirmary for Diseases of the Skin, as early as 1837. Henry Daggett Bulkley was also president of the New York Academy of Medicine and the New York County and State Medical Societies. It was at his home, 42 East Twenty-Second Street, that the New York Dermatological Society was founded on May 18, 1869. He died in 1872.

His son, L. Duncan Bulkley, studied at the Hôpital St. Louis, after his graduation from the College of Physicians and Surgeons in 1869. On his return to New York he became most active in dermatology. He won the Alvarenga prize in 1891 from the College of Physicians of Philadelphia, with his monograph "Syphilis in the Innocent." He wrote several hundred articles and six or eight textbooks, mostly devoted to dermatotherapy, in which he had a deep interest. He was

one of the founders of the American Dermatological Association, which was formed in Philadelphia on Sept 6, 1876, at the University of Pennsylvania, and he was the secretary of its first annual meeting, which was held in Niagara Falls, N Y, on Sept 4, 1877

Dr J Francis Aitken was the hospital's first house physician, serving from Dec 1, 1883 to Dec 1, 1884 He joined the medical staff immediately on the completion of his internship and served continuously until his death, on Aug 3, 1930 For forty-four years he attended the hospital three days a week During the twenty years that I served with him he never failed to be present the minute the clinic was opened, he rarely if ever missed a day, despite bad weather and no matter how badly he might have felt at times Dr Aitken was a master clinician and an expert in "sight diagnosis" He always remained free from hospital politics, and when he did take sides it was always for the oppressed one He had a great and kindly heart, he loved life, his specialty and his fellowmen

Dr George Henry Fox served the hospital from 1883 to 1913 and also gave it of his best, which is no faint praise to any one fortunate enough to have known Dr Fox and his splendid career, which began seventy years ago In that interval Dr Fox received every possible dermatologic honor, the enumeration of which would in itself make a long article There is no question that the successful passage of the difficult early years of the hospital was due in large part to the devotion and self sacrifice of Drs Fox, Bulkley and Aitken

Other medical officers of the hospital in its first year were Drs Daniel Lewis, W T Alexander, Robert F Weir and Edward L Keyes Among the consultants were such famous men as Drs W H Draper, Fordyce Barker, T Gaillard Thomas, E G Janeway, Alfred L Loomis and Abraham Jacobi

In 1886 a country branch at Fordham Heights, near High Bridge, was opened for the patients with cancer, in order to give them the benefit of life in the country Besides the main house there were a number of separate cottage pavilions The city hospital at 243 East Thirty-Fourth Street was retained as a dispensary and hospital for cutaneous diseases Its fame increased with the years, and by 1896 the usefulness of the hospital had long outgrown its building New quarters were therefore imperative, and its board of governors decided to build, on Second Avenue and Nineteenth Street, a structure which would amply hold the increased attendance This new building (the present location) was erected in 1897 and occupied in 1898

In the hospital's first year at the new site 1,788 patients were treated in the dispensary and 205 patients in the wards Little did the men responsible for its career then realize that thirty-three years later in the same building 29,597 people would apply for relief in its dispensary alone

In 1890 Dr. Henry H. Whitehouse joined the medical staff and served the hospital faithfully for the ensuing thirty-nine years. Next to Dr. J. F. Aitken, he has had the honor of having served longer than any one else on the staff. He was an office associate of Dr. L. Duncan Bulkley for many years. Dr. Whitehouse also served as president of the medical board and was untiring in his service. He was on the consulting staff of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital at the time of his death on Aug 24, 1938.

As the years have passed, many of the well known dermatologists, some of whom have since gained well deserved fame, have served the hospital at various times. Among those may be mentioned Dr. George T. Elliot, professor of dermatology at Cornell for many years, Dr. George T. Jackson, who later occupied the chair of dermatology at the College of Physicians and Surgeons, Dr. Howard Fox, professor emeritus of dermatology and syphilology at the New York University College of Medicine, Dr. William B. Trimble, who preceded Dr. Fox in the chair of dermatology at Bellevue Hospital Medical College, Dr. Udo J. Wile, professor of dermatology and syphilology at the University of Michigan, Dr. Edward P. McGavock, professor of dermatology at the Medical College of Virginia for many years; Dr. Fred Wise, professor of clinical dermatology and syphilology at the New York Post-Graduate Medical School and Hospital, and Dr. A. Schuyler Clark, who served the hospital from 1905 to his sudden and untimely death on March 22, 1929. Among the surgeons were such well known men as Daniel Lewis, Willy Meyer, Franz F. Torek, William Seaman Bainbridge and George Semken.

THE NEW YORK POST-GRADUATE MEDICAL SCHOOL AND HOSPITAL

The establishment of postgraduate instruction in medicine in New York is an interesting subject. In 1809 the New York Hospital threw open its wards to both medical students and graduates in medicine. In 1822 the New York Eye and Ear Infirmary and in 1853 the New York Ophthalmic Hospital did the same thing, but it was not until 1877 that the New York Eye and Ear Infirmary definitely stipulated that all its students must present the degree of Doctor of Medicine.

The embryonic life of the New York Post-Graduate Medical School and Hospital began seven years before its birth, which occurred on Nov. 6, 1882. Those responsible for this prenatal life were: Drs. W. A. Hammond, James L. Little, D. B. St. John Roosa, Fred R. Sturgis, M. R. Patten, W. S. Gourley and that great dermatologic pioneer, Henry G. Piffard. These physicians conceived the idea of post-graduate instruction in New York as early as 1875, for in that year they

formed a postgraduate faculty at the New York University Medical College, and they were permitted to grant certificates to physicians completing the course. Their success was so great that by 1881 they realized the inadequacies of the conditions under which they were working and the necessity of a separate building and complete segregation from the undergraduates. The University was not prepared to accede to these just demands, so on April 4, 1882, this group resigned, as Roosa stated at the time, "Like Abraham we did not know the country to which we were going, but the Lord had ordered it and we went." Unsuccessful overtures were made to Cornell and even to Princeton. Frequent meetings were held during the summer and fall of that year. At a meeting on June 27 a committee of organization was formed with Dr. Hammond as chairman, Dr. Sturgis as a member and Dr. Satterthwaite as secretary.

The school opened on Nov. 6, 1882, at the College of Pharmacy on East Twenty-Third Street. One hundred students matriculated in its first year. The faculty consisted of nine professors, eight associate professors and eight instructors. The school grew so rapidly that by its fourth year commodious quarters were secured at 226 East Twentieth Street, and all the rooms above the second floor were devoted to hospital use. Much of this success was due to the unemitting efforts of Dr. D. B. St. John Roosa, one of the outstanding figures in American medicine. Roosa was born in Bethel, N. Y., on Sept. 4, 1838. His college education was acquired at Yale University, and he received the degree of Doctor of Medicine from New York University in 1860. He immediately volunteered his services in the Civil War and as an assistant surgeon served his country faithfully until the end of hostilities. He then spent a year in Vienna in postgraduate work. On his return to New York he gained early recognition as a specialist in diseases of the eye and ear. He became professor of ophthalmology and otology in the medical department of New York University in 1875 and wrote some excellent treatises on his specialty, but apparently one of his great interests in life was the New York Post-Graduate Medical School and Hospital. He was one of its founders, its first professor and its first president, from its beginning in 1882 to his death on March 8, 1908.

The greatest difficulty in the early years of the school was naturally a financial one. Its circumstances were so straitened that its first faculty contributed \$50 each to meet its first expense. However, their vision was keen, for in May 1894 a six story building on Second Avenue and Twentieth Street was occupied, and on Jan. 11, 1912 the present twelve story building was erected. In 1924 the United Hebrew Charities Building at Twenty-First Street and Second Avenue was purchased and renamed the James F. McKernon Building in honor of the president of the school. The New York Post-Graduate Medical School and Hospital and the New York Skin and Cancer Unit now occupy the

entire front on Second Avenue between Nineteenth and Twenty-First streets, with much adjacent property on the side streets

The department of dermatology and syphilology of the New York Post-Graduate Medical School and Hospital at its inception was a part of the department of genitourinary and venereal diseases, under the leadership of Dr Frederick R Sturgis, and it was established at the same time as the school As Dr Sturgis' time was completely taken up with the teaching of genitourinary diseases, it is logical to suppose that Dr. Henry G Piffard took up the teaching of cutaneous diseases, this supposition is further strengthened by the fact that he was a member of the original postgraduate faculty at New York University in 1875 and an active leader in the secession of this faculty from the University in 1882 He was on the first list of professors of the New York Post-Graduate Medical School when it was founded on Nov 6, 1882, and as far as I can ascertain, Piffard limited his work entirely to dermatology. Among his many activities besides teaching was the publication in 1868 of an excellent translation of Hardy's "The Dartrous Diathesis or Eczema and Allied Affections" In 1876 he published his well known "Elementary Treatise on Diseases of the Skin" It was the second textbook on cutaneous medicine to be published in America and was by no means "elementary," as the modest title suggests, but on the contrary was a masterly presentation of the dermatologic knowledge of that day, interspersed by Piffard's practical knowledge of the subject In 1881 "A Treatise on the Materia Medica and Therapeutics of the Skin" appeared Piffard was one of the founders of the New York Dermatological Society in 1869 and was present at the organization of the American Dermatological Association on Sept. 6, 1876. Piffard was intensely human and had a brilliant mind and a warm heart One of my most pleasant recollections was my long and friendly association with Dr George Henry Fox After lunch or dinner cigars were lighted, and Dr Fox's anecdotes of his friend Piffard were a joy to hear As they were intimates until Piffard's death on June 8, 1910, the stories were many and varied

It is interesting to note that as early as 1889 the New York Post-Graduate Medical School and Hospital recognized the advisability of full time instruction in dermatology and its separation from genitourinary diseases. A separate dermatologic department was at long last organized, with George Henry Fox as professor, G T. Jackson and F B Carpenter as instructors and C W Cutler and F J Levisieur as clinical assistants Thus was launched on its enviable career a great factor in the postgraduate instruction of dermatology in America

George Henry Fox, the head of the new department, had already gained a high reputation in his specialty He was at the head of his own service at the New York Skin and Cancer Hospital and was also

professor of dermatology at the College of Physicians and Surgeons. He had already published his celebrated "Photographic Atlas of Diseases of the Skin" and had been one of the principal founders of the American Dermatological Association in 1876. An anecdote which he related to me and which appears in his delightful "Reminiscences"¹ refers to the New York Post-Graduate Medical School and Hospital and belongs in this relation.

On Thanksgiving Day a "spread" was prepared for the students. Around the large lecture room were two rows of arm chairs and in the center a table was laden with turkey, sandwiches, etc. Doctor Roosa urged a number of the faculty to be present on this occasion and act as a reception committee. I was on hand promptly and while my inclination was to talk with Rice, Sturgis, and others, I felt it my duty to try and be as agreeable as possible to some of the students who were strangers to me. Seeing a vacant chair in the circle I took it and began a conversation with the doctor at my left. He proved to be from Montana and entertained me with an interesting account of the mining industries there and of his wife and children. Then it occurred to me that the doctor at my right who was silently stowing away a plate full of salad might perhaps feel slighted if I did not pay him a little attention. So I turned and inquired as pleasantly as possible "Are you from the West?" Swallowing a spoonful of salad he slowly and scornfully said, "No, I am the Second Assistant in the Orthopedic Department." Great Heavens, what should I do to repair such a humiliating blunder. But before I could frame the proper apology he turned to me and to my great surprise asked "Where are you from?" As Vice-President of the institution I was paralyzed for the moment, but quickly realized that my friend had evidently studied at some other college than the "P and S" and not being interested in dermatology we were both in the same boat, neither one of us having ever seen or heard of the other.

Dr. Fox died on May 3, 1937, in his ninety-first year, and in his long span of life he had received a host of dermatologic honors. Besides his great friendliness, sociability and joviality, he had another but much rarer attribute, namely, modesty. On the many occasions that we were together I have never heard him speak of his own honors, but he was always ready to speak of those around him who had attained a high degree of proficiency in the specialty he had so greatly loved. Another of Fox's most lovable traits was the extraordinary friendship and interest which he manifested for the young tyros of his specialty. His willingness to help them in every way possible was expressed without the slightest trace of condescension. As Pusey rightly stated, "He was perhaps the friend of more American dermatologists than any other one of his generation." After Dr. Fox had spent some years as professor and vice president at the New York Post-Graduate Medical School and Hospital a serious disagreement arose as to the management of its affairs, and Dr. Fox resigned.

¹ Fox, G. H. *Reminiscences*, New York, Medical Life Press, 1926.

He was succeeded by Dr Robert W Taylor, one of the organizers of both the New York Dermatological Society and the American Dermatological Association. Known to his intimates as "Bob" Taylor, he was a man of forceful opinions and a born fighter. He was such an avid reader of current literature that he could not only quote authors but give their opinions verbatim. He had a remarkable memory and could frequently relate years later clinical histories of patients, even recalling their names. In discussions he was fond of high-sounding names and particularly liked the word "epiphenomenon." Because of his extraordinary memory and complete knowledge of the current literature, he must have made a splendid teacher.

Dr George T Elliot was next in line as head of the department. He deserved the honor, as he had served as an assistant from the inception of the service under Professor Sturgis. He later became professor of dermatology and syphilology at Cornell University and from 1882 to 1901 was Dr L Duncan Bulkley's chief of clinic at the New York Skin and Cancer Hospital. Dr Charles W Allen (1854 to 1906) also served as professor of dermatology. He devoted much attention to roentgenotherapy and phototherapy and paved much of the way for others in those respective fields. He was jovial and had an overflowing good humor. He died prematurely at Gibraltar while on his way home from the Fifth International Dermatological Congress at Lisbon, to which he was a delegate from the American Dermatological Association.

Dr Sigmund Pollitzer (1859 to 1937) served the school as professor of its department of dermatology from 1895 to 1915. He was an outstanding figure in the dermatologic world. Pollitzer was graduated from the college of Physicians and Surgeons of Columbia University in 1884. After graduation he left for Europe and did research work in physiology in Heidelberg, Germany, and bacteriology in Fresenius' laboratory in Weisbaden, Germany, later he took up special work in Virchow's laboratory and at this time did much original work in physiologic chemistry. It was not until 1889 that he entered on his life's work, first at Unna's clinic and then as an assistant to Sir Malcolm Morris, where for a time he edited the *British Journal of Dermatology* under Morris' direction. From London he went to Paris, and there began a life-long friendship with Darier, whose textbook he translated into English in 1920. Pollitzer made approximately seventy-one contributions to dermatologic literature. Among the best remembered are his monographs on acanthosis nigricans, xanthoma of the eyelid, hydradenitis suppurativa, parakeratosis variegata, arsphenamine for the treatment of syphilis and serum therapy and serum diagnosis in syphilis. Pollitzer was an expert histopathologist. He was a strict parliamentarian and was especially critical of long-winded discussions lacking concrete facts. In such instances he could in a few words of polished

English and in well chosen scientific terms completely smother the unhappy speaker with unassailable facts, from which there was nothing else to do than to retire in confusion. Pollitzer in acting thus did much good service, for he deflated the ego of the usual group of know-it-alls who frequent every dermatologic meeting. In his home and with his friends he exuded kindness, generosity and simplicity. Despite his honors and his high ability, he was always the earnest student. Pollitzer belongs to that small group of physicians who have placed dermatology on a sound, dignified and scientific basis. I have always considered the friendship Pollitzer evinced for me one of the great satisfactions of my life. He is sadly missed at the meetings of the Section of Dermatology and Syphilology of the New York Academy of Medicine, to which organization he was devotion itself.

Dr A. Schuyler Clark (1874 to 1929) was for nine years a professor in the department of dermatology at the school. He and Dr Henry H. Whitehouse (1864 to 1938), who served as professor and executive officer of the department from 1914 to 1925, furnish additional evidence of the cordial relations existing between the New York Post-Graduate Medical School and Hospital and the New York Skin and Cancer Hospital, as both men were active in Dr Bulkley's service at the latter institution. Dr Whitehouse succeeded Dr George Henry Fox at the New York Skin and Cancer Hospital as head of one of the clinics there. He served for thirty-eight consecutive years at that hospital and eleven years at the New York Post-Graduate Medical School and Hospital. In addition, he was elected president of the medical board of the New York Skin and Cancer Hospital in 1928 and served for seven years. Whitehouse greatly enjoyed teaching, and his lectures were carefully prepared and lucidly presented to the matriculates, who always listened to them attentively. He was a fine clinician and skilled in therapy, a fact easily appreciated in consideration of the thirty-eight years spent in the largest dermatologic clinic in America under the tutelage of physicians like L. Duncan Bulkley, George Henry Fox and George T. Elliot. Whitehouse's personality was delightful. At the dinner table, in debate, while teaching and in conversation, whether dermatologic or lay, he was always refreshing and affable. He was a staunch friend, and if he did dislike any one it was for a logical reason and he did not hesitate to give vent to that reason to the man himself. At the time of his death he was the senior member of the New York Dermatological Society, which he had served as president for three different terms. He is greatly missed by those who were his intimates.

The year 1928 marked a new era for the department of dermatology and syphilology at the New York Post-Graduate Medical School and Hospital. When Whitehouse resigned in 1925, A. Schuyler Clark became the head of the service and remained in that institution until

1928 In the meantime, Dr John A Fordyce died on June 4, 1925, and George M MacKee, who had been his chief of clinic at New York University and had followed him as chief of clinic at the College of Physicians and Surgeons, had built up a splendid dermatologic organization at the Vanderbilt Clinic, more than doubling the attendance of patients at the clinic, thereby giving it a world-wide reputation Every one expected that MacKee would succeed Fordyce as professor of dermatology and syphilology at the College of Physicians and Surgeons, as he had built up a clinic second to none in the United States, had himself done an enormous amount of original work and occupied an enviable position in the dermatologic world, but politics ordered otherwise, and he did not receive the appointment He and his staff stuck to the service until well beyond the appointment of Fordyce's successor, whereupon he and most of his staff resigned from the Vanderbilt Clinic Dr A. Schuyler Clark resigned his post at the New York Post-Graduate Medical School and Hospital, and MacKee and his original Vanderbilt Clinic staff took it over The change took place in 1928 In their first year eighteen postgraduate students matriculated MacKee, a born organizer, soon had the clinic running at top efficiency, and the increase in the reputation of the department caused a great increase in matriculates At the time of the affiliation with the New York Skin and Cancer Hospital in 1934, MacKee was the logical choice as director of the combined institutions The entire main building of the Stuyvesant Square Hospital was renovated and altered in order to create a complete self-contained dermatologic unit The building consists of four stories and a basement In the basement the roentgenotherapy, phototherapy, physical therapy and photographic departments are located On the first floor are the offices, the reception rooms for patients, the files and the department of syphilology The second floor is devoted to new patients, a large air-conditioned lecture hall, with ample dressing rooms, and the office of the chief of clinic The third floor houses the old patients, dressing rooms and the department of allergy On the fourth floor are the surgical department, the department of mycology and the histologic laboratory It will therefore be seen that the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital is a complete unit, in which all divergent branches of dermatology, investigative and otherwise, can be studied and cared for under a single roof Dermatologic beds are taken care of in two wards of the hospital, which are exclusively for dermatologic use

Thus the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital has entered on a phase which can but enhance the previous splendid record of dermatologic accomplishment made by the United States as a whole, but one must keep in mind that,

after all, these accomplishments would amount to little, were it not for the ground work done by pioneers of yesterday, who in turn received the flaming torch of dermatologic knowledge from Bielt, Cazenave, Devergie and Bazin of France, Willan, Bateman, Wilson and Tilbury Fox of England, Unna of Germany and that immortal master, Ferdinand von Hebra of Vienna, and his associates Auspitz, Kaposi and Neumann. To them, after all, remains the glory of molding American dermatology, which today has grown to lusty manhood, stands on its own feet, and in teaching, research and clinical facilities is second to those of no country in the world.

THE VESICANT CHEMICAL WARFARE AGENTS

LEON GOLDMAN, MD

AND

GLENN E CULLEN, PH D

CINCINNATI

In the World War there were introduced irritant chemical compounds which acted primarily by blistering the skin or mucous membranes. Although known to chemists since 1866, it was not until July 22, 1917 that the first compound, dichloroethylsulfide (mustard gas), was used on a large scale as a casualty-producing agent. Within three weeks after the introduction of this gas by the Germans, the British forces had 14,276 members injured, of whom 500 died¹. In the American Expeditionary Forces in the World War there were 27,711 casualties from mustard gas, with only 599 deaths. Of this large number of casualties there were only 4 cases of loss of sight of both eyes². Whether the blindness was due to mustard gas or to other gases in all of these 4 cases is not known. Although primarily sternutators, some of the other war gases, such as diphenylchloroarsine (Clark I), phenyldichloroarsine, ethyldichloroarsine (Dick), diphenylcyanoarsine (Clark II) and methyldichloroarsine (Methyldick), also blistered the skin. There is some controversy as to whether the efficient methyldichloroarsine was used actually in warfare toward the end of the war.³

At the Ninth International Congress of Military Medicine and Pharmacy, in Bucharest, Rumania, in June 1937, it was claimed, "It is likely that in future war the use of gas will be made on a larger scale"⁴. Flury⁵ has stated that the subject of the chemical warfare agents "will present to the dermatologist a good many unsolved questions and will stimulate him to concern himself more with this field."

From the Department of Dermatology and Syphilology of the University of Cincinnati College of Medicine and the Research Foundation of the Children's Hospital

1 Prentiss, A. M. Chemicals in War, New York, McGraw-Hill Book Company, Inc., 1937.

2 Gilchrist, H. L. A Comparative Study of World War Casualties from Gas and Other Weapons, Washington, D. C., Government Printing Office, 1928.

3 Sartori, M. The War Gases, New York, D. Van Nostrand Company, Inc., 1939.

4 Bainbridge, C. W. S. Report on Ninth International Congress of Military Medicine and Pharmacy, Mil Surgeon 82-225 (March) 1938.

5 Flury, F. Dermatologische Probleme im Luftschutz, Med Klin 30:13 (Jan 5) 1934.

CLASSIFICATION

There are many vesicant agents, but because of the military tactical requirements and the limitations of manufacturing and of transportation facilities, there are at present relatively few that meet all these requirements. From a physiologic aspect these vesicant gases may be classified briefly as causing (1) primarily local tissue irritation (the sulfur compounds) and (2) combined local irritation and systemic intoxication (the arsine compounds).

Dichloroethylsulfide is known as mustard gas to the Americans and English, as yperite to the French and as "*Senfgas*," mustard gas or *Lost* to the Germans. *Lost* is derived from the first two letters of the names of the German investigators of this gas (Lommel and Steinkopf). Mustard gas and lewisite (chlorovinylchloroarsine) are known to the Germans also as *Gelbkreuzgruppe*, because of the manner of marking the shells containing these gases. On the basis of the rapidity of production of bullae, the severity of the local reaction and the time required to heal the local lesions, Prentiss¹ has classified the gases in descending order

- (1) mustard gas
- (2) lewisite
- (3) phenyldichloroarsine
- (4) methyldichloroarsine
- (5) ethyldichloroarsine
- (6) phenyldibromoarsine
- (7) dibromethylsulfide

Unlike those war gases which cause primarily severe damage to the lung, such as phosgene (carbonyl chloride) and trichlormethylchloroformate (Perstoff), most of the vesicant agents have the important physical characteristic of persistence, i. e., the chemicals remain in the place where they are discharged for some time. For instance, mustard gas, because of its low volatility, can remain in the summer for five to ten days in the open and from two to three weeks in the woods, in the winter the gas can remain for several weeks both in the open and in the woods. Mustard gas, when pure, freezes at 14 C (57 F). Because of this fact the presence of the mustard gas may not be detected in cold weather. In addition to temperature, other elements of weather, such as wind, clouds and air pressure, have some influence on the concentration of mustard gas vapor. Mustard gas will penetrate paint, woodwork, porous materials, shellac, paper, wax, leather and ordinary clothing. Oilskin clothing and synthetic rubber materials are penetrated slowly. Metals, glass, glazed earthenware and cellulose coverings are

resistant to the gas. The presence of mustard gas on a person or object is spoken of as "contamination" The persistence of dibromethylsulfide on the ground is said to be greater than mustard gas only in dry weather No definite data are available on the persistence of diiodethylsulfide

Physical Properties of the Vesicant Gases

Agent	Physical State	Odor	Volatility at 20 C (68 F)	Solubility	
				Water	Other Solvents
Mustard gas	Oily liquid, brownish, colorless when pure	Garlic or horse radish	0.625 mg per liter	0.047 Gm per liter 0.069 Gm per liter (25 C)	Very soluble in various hydrocarbons and organic solvents (kerosene, gasoline, absolute alcohol, carbon tetrachloride, chloropicrin, petrolatum and paraffin wax.)
Dibromethylsulfide	White crystals, melting point 310-340 C	?	400 mg per liter	Insoluble	Soluble in alcohol, ether and benzene
Diiodethylsulfide	Bright yellow prisms, melting point 62-68 C	?	?	?	?
Lewisite	Colorless liquid	Geranium	2,300 mg per liter	0.50 Gm per liter	Readily soluble in benzene, absolute alcohol, olive oil and kerosene
Ethyl-dichloroarsine	Liquid, colorless first, then slightly yellow	Fruity	20,000 mg per liter	1.00 Gm per liter	Readily soluble in alcohol, ether, benzene and acetone
Methyl-dichloroarsine	Colorless liquid	?	74,440 mg per liter	1.00 Gm per liter	Soluble in ordinary organic solvents
Phenyl-dichloroarsine	Liquid, colorless when pure, then yellow	?	404 mg per liter	Insoluble	Soluble in ordinary organic solvents
Diphenyl-chloroarsine	Dark brown liquid	Shoe polish	0.69 mg per liter	2.0 Gm per liter	Readily soluble in carbon tetrachloride, phosgene, chloropicrin and phenyldichloroarsine 20 Gm per 100 cc absolute alcohol ^a , 50 Gm per 100 cc kerosene, 100 Gm per 100 cc benzene, 14 Gm per 100 cc olive oil
Diphenyl bromarsine	White crystals	Similar to diphenylchloroarsine			
Diphenyl-cyanarsine	Colorless prisms	Mixed garlic and bitter almonds	0.0002 mg per liter	Sparingly	Readily soluble in alcohol, benzene, chloroform and ether
Diphenyl-amine-chloroarsine	Green or brownish solid	Practically odorless	0.02 mg per liter	Practically insoluble	Sparingly soluble in organic solvents

Lewisite as such is much less persistent than mustard gas, it lasts in the summer only twenty-four hours in the open and one week in the woods. The persistence of the other chlorovinyl arsines has not been reported. The aromatic arsines are nonpersistent, the significant concentrations lasting several minutes to several hours.

Hydrolysis is important from both a military and a medical standpoint, for hydrolysis may render the agent, after a period, either harmless or still dangerous. The latter result is produced by a hydrolysis product

being of itself toxic. Mustard gas in contact with water is sparingly soluble. It hydrolyzes at a rate depending on the temperature and the rate of stirring. The hydrolysis products are hydrochloric acid and thiodiglycol. In contrast to mustard gas, lewisite is rapidly decomposed in contact with water even at ordinary temperature, with the formation of hydrochloric acid and an oxide of lewisite, which itself is nonvolatile and vesicant. Dibiomethylsulfide is more rapidly decomposed by water than dichloroethylsulfide. The hydrolytic activity of diiodoethylsulfide is not reported at present. The aromatic arsines hydrolyze easily, producing nonvesicant but nauseating arsenic trioxide compounds.

To be able to recognize these vesicants and to understand their action and the therapy of the lesions produced, it is necessary to know more of the various physical properties of the gases. As a rule, whenever mustard gas is in sufficient concentration to be recognized by its characteristic odor casualties may be caused by exposure over prolonged periods.

CLINICAL SYMPTOMS

The clinical picture of the conditions caused by this vesicant group as a whole may be divided into the following stages: (1) the latent period, (2) the period of acute reactions and (3) the period of subacute and chronic reactions.

The duration and intensity of the reactions vary according to the character and concentration of the chemical agent used, the sensitivity of the patient and, for the skin, the area or areas of skin involved. Actual war experience has given the picture of the lesions caused by mustard gas and some of the aromatic arsines; the lesions produced by the aliphatic arsines and other compounds have been studied chiefly through various experimental procedures. Apparently no new types of vesicants were used in the Italo-Ethiopian War.

In regard to the clinical course of the mustard gas burn, the latent period is an important phase, because it is only in this stage that the treatment may prevent or reduce appreciably in severity any subsequent lesions. The latent period varies for mustard gas from about two to six hours. Generally, the longer the latent period the less severe will be the subsequent reaction. During this phase the mustard vapor or liquid remains on the cutaneous surface approximately three minutes, depending on the amount. Then it is slowly absorbed (through great solubility in cutaneous lipids?). The deep penetration into the skin is said to occur through the follicles and the sebaceous glands. Absorption is more rapid and more intense if the cutaneous surface is covered and if the skin itself is warm and moist. The end of the latent period is marked by burning and itching.

Erythema is the first sign of the period of reaction. It occurs especially in the axillary and crural areas and on the scrotum, neck, elbows and eyelids and may be faint or intense. Erythema may be the only reaction and may subside entirely in twenty-four hours.⁶ Nikolsky's sign may be obtained at times over the erythematous areas. However, the more common course is for vesicles and bullae to develop gradually after eight to twelve hours. The height of the bullous reaction is two and a half to three days. Secondary infection is not uncommon. The fluid from the bulla does not of itself produce fresh vesicles. In lesions caused by the drops or splashes of the liquid chemical and not by the vapor, the vesicles are arranged in a characteristic peripheral fashion about a central area of induration. Around the vesicles may be found an irregular zone of whitish discoloration (*der ananusche Bezirk*).⁷

The raw, oozing surfaces heal slowly. The scar is usually smooth. Contractures may occur in scarring over joint surfaces. Various forms of pyoderma are not uncommon during the subacute and chronic phases. Even with the extensive cutaneous lesions caused by mustard gas itself there are usually no systemic reactions save vague malaise, anorexia, low grade fever and a decreased amount of hemoglobin in the blood. Of course, in this subacute and chronic phase secondary infection of the cutaneous lesions themselves may occur and produce the usual symptoms and signs of sepsis. In the postmortem study of victims of uncomplicated mustard gas poisoning, essentially nonspecific toxic changes have been found in the viscera.

Interesting also to dermatologists is the fact that widespread brownish pigmentation may occur, following even mild erythema, and may last for weeks. It is reported that the brownish pigmentation may arise also without preceding erythema, and occasionally this form of discoloration may be distributed over the body in large irregular blotches.⁷ Severe pruritus may be present for some time after all lesions have healed. Under certain rare circumstances mustard gas may produce such a deep burn of the skin that no bulla is formed. The ulceration so resulting may require months to heal. Although it is frequently not possible to classify them, Muntsch⁷ stated that there are four general types of cutaneous reactions. (1) simple erythematous, (2) pigmented and exfoliative, (3) eczematous, and (4) edematous, bullous, ulcerative and necrotizing.

Microscopically, the earliest changes in the epidermis are distortion and shrinkage, and in the cutis, dilatation of the vessels, with some perivascular infiltrate and edema of the pars papillaris. From the histologic study of cutaneous lesions one-half hour after the application of

6 An Atlas of Gas Poisoning, London, His Majesty's Stationery Office, 1938

7 Muntsch, O. Leitfaden der Pathologie und Therapie der Kampfstoffkrankungen, Leipzig, Georg Thieme, 1939

mustard gas, Warthin and Weller⁸ stated, "in the neighborhood of the hair follicles the corium is affected more deeply than elsewhere, showing a distinct penetration through the hair follicles" Following these changes spongiosis develops Definite intraepidermal vesicles may be seen in two hours The inflammatory infiltrate in the cutis increases, and many eosinophils⁷ are found The necrotic changes in the epidermis continue, and soon extensive crusting is produced There may be considerable hemorrhage in deeper tissues, but vessel thromboses are not great and occur chiefly at the edge of the ulceration of the skin In the healed area the pigmentation is found to be chiefly chromatophore In a necrotic cutaneous lesion from a patient who died of mustard gas burns Warthin and Weller⁹ noted sebaceous gland necrosis, with islands of regenerating squamous epithelium marking the site of these glands The other significant feature of a picture of essentially severe and deep destruction of skin with attempts at regeneration was a sparse inflammatory infiltrate save where secondary infection was present Rehbein¹⁰ has commented on the histologic similarity of the bullae caused by mustard gas and those of pemphigus From a study of animal experimentation Dorffel and Popping¹¹ were impressed with the close histologic association of mustard gas dermatitis and acute roentgen dermatitis They found no similarity of mustard gas dermatitis to severe acid burns of the skin They mentioned, in addition, dyskeratotic changes in the healing phase Such changes have not been described for the human skin There have been no reports of a tendency toward malignancy in mustard gas lesions Moreover, Visser and Seldam¹² succeeded in inhibiting malignant growth from tar in mice by adding 0.5 per cent mustard gas to the tar The anticarcinogenic activity of mustard gas had been noted also by Berenblum and Wormall¹³ and by Jány and Seller¹⁴ It is interesting also that mustard gas solutions injected subcutaneously, intramuscularly and intraperitoneally cause locally only intense edema and no necrosis The reason for the absence of local

8 Warthin, A. S., and Weller, C. V. The Pathology of the Skin Lesions Produced by Mustard Gas (Dichlorethylsulphide), *J. Lab. & Clin. Med.* 3: 447 (May) 1918

9 Warthin, A. S., and Weller, C. V. The General Pathology of Mustard Gas (Dichlorethylsulphide) Poisoning, *J. Lab. & Clin. Med.* 4: 265 (Jan) 1919

10 Rehbein, cited by Muntz⁷

11 Dorffel, J., and Popping. Tierexperimentelle Untersuchungen über die Veränderungen der Haut nach Aetzung mit Dichloräthylsulfid (Gelbkreuz) und Mineralsäuren, *Virchows Arch. f. path. Anat.* 295: 1, 1935

12 Visser, J., and Seldam, R. E. J., cited by Schwartz and Tulipan¹³

13 Berenblum, I., and Wormall, A. The Immunological Properties of Proteins Treated with BB' Dichlorodiethylsulphide (Mustard Gas) and BB' Dichlorodiethylsulphone, *Biochem. J.* 33: 75 (Jan) 1939

14 Jány and Seller, cited by Berenblum and Wormall¹³

necrosis is thought to be rapid local absorption of the irritant, unlike the slow absorption which occurs in the skin ¹⁵

Since mustard gas is universally irritant, lesions of any unprotected surface may occur. The commonest of these is in the eye, where the conjunctivitis varies from simple acute to chronic proliferative. There is described a xanthoma-like pigmentation which develops near the outer or inner sclerocorneal junction or over the corneal limbus ¹⁶. There may be severe body burns without eye burns if the eyes have been protected by a good gas mask. Ulceration of the lips, tongue and pharynx may occur also. Small burns in the mouth and on the tongue resemble aphthous ulcers. Laryngitis with long-continued hoarseness may result also. If a sufficient concentration is inspired, an ulcerative tracheo-bronchitis with secondary severe bronchopneumonia may occur. It is bronchopneumonia which is chiefly responsible for the deaths from mustard gas.

The effects of lewisite differ essentially from those of mustard gas in that the latent period is much shorter (fifteen to thirty minutes), there may be associated sneezing and nasal irritation, the bullae increase in size more rapidly, the contents of the bullae are clearer, and secondary infection of the bullae is much less frequent. In addition, because of the arsenic content, varying degrees of arsenical poisoning are produced by the cutaneous lesions caused by lewisite. Vedder ¹⁷ claimed that a man of average weight would die if 1.4 cc of lewisite were splashed on his skin and he received no treatment. The pigmentation following lewisite lesions is believed by some to be more intense than that following mustard gas lesions ¹⁸. On the other hand, Héderer and Istin ¹⁹ stated that in the absence of secondary infection, the lewisite lesion may heal with little or no pigmentation. Other arsenical warfare agents also act more quickly than mustard gas. The differences between the various arsenicals are essentially quantitative. Ethyldichloroarsine produces paronychia more commonly than the other agents.

15 Smith, H. W., Clowes, G. H. A., and Marshall, E. K., Jr. On Dichloroethylsulfide (Mustard Gas). IV. The Mechanism of Absorption by the Skin, *J. Pharmacol. & Exper. Therap.* **13**:1 (April) 1919.

16 Warthin, A. S.; Weller, C. V., and Herrmann, G. R. The Ocular Lesions Produced by Dichloroethylsulphide (Mustard Gas), *J. Lab. & Clin. Med.* **4**:785 (Oct.) 1918.

17 Vedder, E. B. *The Medical Aspects of Chemical Warfare*, Baltimore, Williams & Wilkins Company, 1925.

18 Hanzlik, P. J., and Tarr, J. The Comparative Skin Irritant Properties of Dichloroethylsulphide ("Mustard Gas") and Other Agents, *J. Pharmacol. & Exper. Therap.* **14**:221 (Nov.) 1919.

19 Héderer, C., and Istin, M. *L'arm chimique et ses blessures*, Paris, J. B. Baillière et fils 1935.

MECHANISM OF THE ACTION OF VESICANTS

The actual mechanism of how these vesicants react with the cells is still unknown. There are, of course, some theories. The oldest one is that of hydrolysis, namely, that the mustard gas is absorbed into the cell, where hydrolysis occurs, and there are formed thioglycol, which is inert, and hydrochloric acid, which destroys the cell. However, briefly, neither clinically nor histologically does the cutaneous lesion due to mustard gas resemble a burn due to strong acid. Another theory mentioned by Flury and Zernik²⁰ is that the intracellular destruction is brought about by oxidation and that other types of foreign body products are formed. They also suggested the possibility that mustard gas acts directly as a capillary toxin, producing dilatation and increased permeability. There is no definite proof for such wide generalizations. The relatively recent theory is that of Cashmore and McCombie,²¹ which claims that the cutaneous lesions are produced by a combination of the mustard gas and the "amino acids present in the skin."

SENSITIVITY OF THE SKIN TO VESICANTS

Every one is agreed that persons vary in their sensitivity to the vesicants, especially to mustard gas. For experimental work either suitable dilutions of the liquid material or the vapor has been used. The liquid has been dropped on the skin by means of a graduated pipet or a fine glass rod. Vapor exposures were made by means of the blower system (quantitative) of Hanzlik and Tair¹⁸ or simply by placing the cutaneous surface over the mouth of a test tube, which is kept at constant temperature and contains cotton plugs soaked with the material. This is similar to the method of Machle and Zwick²² for testing the skin to gasoline vapors. The "Dunstprobe" method of Miescher²³ could be used for the study of the effect of mustard gas vapor on the skin. In general, the vapor tests have been preferred because the results are more uniform and milder. For the concentration of the solution for direct application to the skin, the titer varies usually from 1:10,000 to 1:100. With 0.01 per cent solution approximately 2 to 3 per cent of white men are found to be "hypersensitive" and 20 to 40 per cent "resistant."²⁴

20 Flury, F., and Zernik, F. *Schadliche Gase*, Berlin, Julius Springer, 1931.

21 Cashmore and McCombie, cited by Berenblum and Wormald¹⁸.

22 Machle, W., and Zwick, K. G. *Gasoline Dermatitis*, M. Bull. Univ. Cincinnati 7:93 (Nov.) 1935.

23 Miescher, G. *Die Dunstprobe beim Ekzem*, Schweiz. med. Wchnschr. 70:93 (Feb. 3) 1940.

24 Marshall, E. K., Jr., Lynch, V., and Smith, H. W. *On Dichlorethyl-Sulphide (Mustard Gas) II Variations in Susceptibility of the Skin to Dichlorethylsulphide*, J. Pharmacol. & Exper. Therap. 12:291 (Dec.) 1918.

Expressed quantitatively by Sartori,³ the average amount of mustard gas for the production of an erythema is 0.12 mg. per square centimeter of skin and for a vesicle, 0.5 mg. per square centimeter of skin. With 0.01 per cent solution 78 per cent of Negroes do not react. Ferri²⁵ found that sun-tanned skin was less sensitive than the untanned skin. Even with high dilution of mustard gas the conventional technic of patch test has not been used. As previously indicated, the cutaneous areas that are relatively thin skin, moist and subject to friction are more sensitive to mustard gas. Ferri²⁵ claims in addition that the skin is more sensitive in summer than in winter. It seems to us that the reason for the differences in intensity of the cutaneous reactions in various areas of the same person may be due to differences simply in the concentration of the mustard gas in those areas. Evaporation of the mustard gas from the cutaneous surface may be prevented by clothing or by the proximity of adjacent cutaneous surfaces and moisture. Repeated exposures to even minute quantities of mustard gas cause a gradually increasing sensitivity to mustard gas, this hypersensitivity may last for some years. This suggests certainly that mustard gas is a strong eczematogenous agent. Among the animals, the guinea pig, dog and rabbit react within the same ranges as man. Data on the horse are conflicting. By means of precipitin and complement fixation tests in rabbits, Berenblum and Wormald¹⁸ found that protein changes were produced by a reaction at room temperature between BB' dichlorodiethylsulfide (mustard gas) and horse serum and between BB' dichlorodiethylsulfone and horse serum. There were no serologic cross reactions between the sulfide-treated and the sulfone-treated proteins. These experiments are some proof for the amino acid theory of the action of mustard gas. The contents of the bulla due to mustard gas have not been used for passive transfer tests.

There has been considerable less work done with the arsines. There are no data available as yet concerning the arsenic sensitivity of the skin following burns with lewisite. With phenyldichloroarsine Sayers and Dudley²⁶ found that a 1 per cent solution (in heavy oil) caused a severe reaction on the skin of the majority of a relatively small group tested.

THErapy

The diagnosis of mustard gas poisoning is made usually by the characteristic odor of the vesicant, brownish oily stains present on the clothing and the patient's history. At present there are no good specific

²⁵ Ferri, G., cited by Schwartz and Tulipan³³

²⁶ Sayers, R. R., and Dudley, H. C. *Toxicology of Phenyldichlorarsine*, Pub Health Rep 53:1292 (July 29) 1938

chemical indicators which are simple to use For effective therapy the diagnosis must be made as soon as possible

From their persistence and penetrating power in clothing and leather, the vesicants deserve the title "chemical lepers" The gas mask will protect only the eyes and the respiratory tract Therefore, the chances for cutaneous lesions are high The physician caring for the patients is in great danger of being poisoned himself unless he is protected from vapors by a gas mask and from contaminated clothing and skin by special oilskin gloves and clothing For military purposes clothing can be rendered resistant to mustard gas, but this cannot be used on a wide scale, especially in civilian life The protective costumes at present are cumbersome and do not permit exertion for any long periods of time The use of protective salves and pastes, such as chlorine mixtures, glycerol²⁷ and cellulose, have not been proved effective or practical The therapeutic agents used chiefly for early treatment are the solvents mentioned in the tables or oxidizing materials The oxidizing agents are various chlorine preparations, such as bleaching powder, chloramine-T, diluted solution of sodium hypochlorite and hydrogen peroxide and permanganate²⁸ One great difficulty with all chlorine preparations is their more or less rapid loss of chlorine If the patient can be seen before the cutaneous absorption occurs (three minutes), the skin must be washed with the solvents or, next best, with soap and water, and the washing rags must be discarded and decontaminated The decontamination of cloth, including bandages (mixed vesicant and shell wounds), can be done by burning, boiling, mixing with solution of sodium hypochlorite, chlorination or exposure to freely circulating air for long periods (summer two to seven days, winter fourteen days) Instruments may be decontaminated by cleansing with methyl alcohol and then boiling

The patient will be seen usually in the latent period At this stage therapy should be instituted, since it may reduce the severity of the irritation The clothing should be removed and the skin washed with the solvents or oxidizing agents, and if there has been no protection of the eyes they should be irrigated with 0.5 to 1 per cent chlorcosane solution of dichloramine-T, followed by boric acid,¹⁶ if the chlorine solutions are not available, a mild alkaline salve may be used The mouth should be rinsed and the throat gargled with warm sodium

27 Klarenbeek, A Protection of the Skin Against Mustard Gas by Means of Cellulose Preparations, *Nederl tijdschr v geneesk* 81.5905 (Dec 11) 1937, abstracted, *J A M A* 110 618 (Feb 9) 1938

28 Hillman, C C Care of Gas Casualties, *Mil Surgeon* 70 529 (June) 1932

bicarbonate solutions The patient must then be watched for twelve hours The oxidizing agents used ordinarily are:

- 1 Bleaching powder paste, made with equal parts of water Rinse from the skin to avoid irritation So-called bleaching powder cream may also be used, 2 parts of bleaching powder to 1 of white petrolatum (of questionable value but recommended in several European countries) Bleaching powder still remains the chief therapeutic agent
- 2 Chloramine-T, 1 to 2 per cent
- 3 Diluted solution of sodium hypochlorite, 0.5 per cent (fresh) Watch the skin for irritation
- 4 Hydrogen peroxide, 2 to 3 per cent
- 5 Potassium permanganate, 1:1,000 to 1:10,000

The value of ferric hydroxide pastes (freshly prepared) for use against the arsines is doubtful The Germans believe them to be worthless Sayers and Dudley,²⁶ however, have shown experimentally in a small group that this material does have some protective value against phenyldichloroarsine Their mixture was made of equal parts of petrolatum and freshly precipitated ferric hydroxide Vedder's¹⁷ mixture was 6 parts of ferric hydrate to 1 of pure glycerin, he claimed that it was permanent if kept in air-tight containers

Even when the actual erythema has occurred, treatment should be continued When the bullae appear, they should be débrided, since those caused by mustard gas are especially prone to infection From the experience of the Dutch Ambulance Service²⁹ in the Italo-Ethiopian War it seemed that tannic acid (3 to 5 per cent) did work in the bullous stage Although it has not been used, it appears as if the compound solution of tannic acid³⁰ would be more practical and, of course, more stable Silver nitrate (10 per cent) could be used after the application

29 Belmonte, A. C., and Winkel, C. W. F. With the Ambulance of the Netherlands Red Cross in Ethiopia, *Nederl tijdschr v geneesk* 80:3289 (July 11) 1936, abstracted, *Schweiz med Wchnschr* 48:1216 (Nov 28) 1936

30 Fantus, B., and Dyniewicz, H. A. Compound Solution of Tannic Acid, *J A M A* 109:200 (July 17) 1937

Potassium chloride.	.	.	.	0.42 Gm
Calcium chloride	.	.	.	0.80 Gm
Salicylic acid	1.00 Gm
Sodium chloride	10.50 Gm
Tannic acid	100.00 Gm
Distilled water, to make	1,000.00 cc			

Mix and permit to stand with occasional agitation until dissolved and filter, if required to dispense a clear solution

of tannic acid to promote more rapid crusting. For the treatment of the ulcers and necrotic areas in the latter phases of these chemical burns, the ordinary remedies may be used. Here, too, diluted solution of sodium hypochlorite may be good, especially for the necrotic tissue, the uninvolved skin should be protected with petrolatum gauze.

Unlike extensive burns of the skin, the patients with vesicant gas burns do not show anhydremia or significant changes in the blood chloride content. Therefore, only with conditions such as secondary sepsis and bronchopneumonia should the general remedies be given. For lesions due to the arsines, adequate fluid intake and intravenous administration of sodium thiosulfate (?) and dextrose may be given to prevent arsenical intoxication. Because of the relatively long and painful convalescence these patients are discouraged and depressed, and measures should be taken to keep up their morale.

When the case is complicated by fractures or gunshot wounds, the surgeon and his assistants must protect themselves from poisoning through contact or inspiring contaminated air. Decontamination of the wounds and extensive débridements are advised.

RESIDUA OF THE VESICANTS

As has been mentioned before, with the large number of casualties and relatively small percentage of fatalities, there is likewise a small percentage of residua. Since mustard gas has been used the most extensively in warfare, the following conclusions refer to it. Follow-up studies have been done in this country by Gilchrist and Matz³¹. The deep cutaneous burns heal with scars which in flexural areas may give rise to contractures. Some patients, percentage unknown, have had sensitive scars for a time. Occasionally, the pyoderma associated with the latter stages may persist for some months in the form of a stubborn furunculosis. With the same time relations, an eczematous condition may develop in some cases, while in others actual chronic dermatitis results from the vesicant. It is not known whether a polyvalent sensitivity develops also.

The small number of cases of blindness caused by mustard gas has been mentioned before. This is relatively much less than the blindness caused by other warfare missiles. Various other chronic deformities of the eyes may result. Chronic bronchitis and its concomitants may follow pulmonary irritation. Actually the incidence of this condition is much less than compensation figures indicate. Pulmonary tuberculosis does not follow, causally, any war gas poisoning. Although

³¹ Gilchrist, H. L., and Matz, P. B. *The Residual Effects of Warfare Gases*. I. Chlorins, II. Mustard, United States War Department, Chemical Warfare Service, 1933.

theoretically gastroenteric ulcers and scarring may follow the ingestion of mustard gas, clinically, at least, such complications are not important. All in all, the "relative humanity" of this form of warfare is easily seen.

INDUSTRIAL HAZARDS IN THE MANUFACTURE OF GASES

Since these compounds are so dangerous, their manufacture is likewise dangerous to the worker. Cole, Driver, Bowen and Cooper³² have recently described a study of 24 workers with cutaneous irritations from the arsines, especially diphenylchloroarsine, and from mustard gas. Idiosyncrasy was obvious even in the small series. Moreover, in 1 chemist urticaria developed from various arsines. The authors have emphasized the fact that cleanliness of the plant and training of the workers will do much to avoid cutaneous reactions. Workers must be trained not only in prevention of all forms of reaction but also in securing early therapy. Not only may there be cutaneous reactions from the war gases, but also contact dermatitis from the chemicals used in the manufacture of these gases³³. Since these war gases are strong poisons, they will be used more and more in civil life for insecticides and the like. Sayers and Dudley²⁶ have mentioned the use of phenyldichloroarsine in oil as a wood preservative. This nonmilitary use of the chemical warfare agents will also give rise to cutaneous irritations which the dermatologist must recognize and prevent.

OTHER PROBLEMS

This review lists only some of the more important phases of the modern study of these vesicants. There has been no description of the lesions in horses and the difficulty of prophylaxis and therapy with these animals. Mustard gas casualties on shipboard present many additional problems³⁴. The subject of mixed traumatic and vesicant wounds was mentioned only briefly, yet toward the end of the last war it was the custom to mix chemicals in many different types of artillery shells. Operating rooms in which patients with wounds due to mustard gas are treated must have special arrangements to protect both personnel and patients. Some of the chemicals used as "tear gases" may also produce vesicles. These chemicals are bromobenzylcyanide, acrolein, chloroacetophenone and phenylcarbylamine chloride.

32 Cole, H. N., Driver, J. R., Bowen, S. S., and Cooper, G. War Gases and Industrial Hazards in Their Manufacture, *Arch. Dermat. & Syph.* **39**:45 (Jan.) 1939.

33 Schwartz, L., and Tulipan, L. A Text Book of Occupational Diseases of the Skin, Philadelphia: Lea & Febiger, 1939.

34 Anti-Gas Precautions for Merchant Shipping, Air Raid Precautions, Handbook no. 7, London, His Majesty's Stationery Office, 1936.

This paper does not include a review of cutaneous lesions from other war materials, such as the deep burns from incendiary bombs (made of iron and aluminum or of magnesium) and from phosphorus, which is used to produce smoke screens

THE FUTURE OF THE VESICANTS

Vesicants as warfare agents will be discarded only when more efficient agents are produced. Mustard gas and lewisite are the most effective materials of today. In 1919 Hanzlik and Tarr¹⁸ reported a study of some 70 vesicant agents which might be used in chemical warfare. At that time mustard gas had the greatest efficiency as a cutaneous irritant. Over twenty years later it still retains that leadership, followed closely by lewisite and the other arsines. No descriptions of new and essentially different compounds have been published recently, but progressive chemical research may soon produce others. The physician is at a disadvantage at present since, because of ignorance of the exact mechanism of reaction, he is forced to use inadequate symptomatic therapy. However, he must keep abreast of such research, since knowledge in advance will do much to dispel unnecessary fear and panic about these materials and will prevent casualties.

CONCLUSIONS

Dermatologists should concern themselves with the problem of vesicant chemical warfare agents, for there is much to arouse their interest in this field. The basic mechanisms involved, the factor of cutaneous hypersensitivities and systemic poisoning from the cutaneous lesions of the arsine group are but a few of the more important questions for the dermatologist. It is because of the various unknown elements about these agents that today there is no adequate defense against the action of the vesicants.

UNUSUAL SEROLOGIC REACTIONS DURING PREGNANCY

REPORT OF A CASE

LOUIS G JEKEL, MD
PHOENIX, ARIZ

The following case report is offered without comment

Mrs M W, white, aged 37, presented herself to Dr P T Brown for antepartum care on July 12, 1938. She had previously been pregnant five times and had given birth at term to 5 normal, healthy children. Her routine obstetric examination indicated that she was normal and healthy. The routine Wassermann and Kahn tests, however, gave positive results. The tests were repeated with the same results in the same laboratory and in a second laboratory. The patient was

Summary of Serologic Reactions of Patient During Pregnancy

Laboratory Number	Date	Results of Serologic Tests			
		Wassermann	Kahn	Kline	Eagle
1	7/12/38	+++	++		
1	7/21/38	+++	++		
2	7/19/38	Positive	Positive		
3	9/ 3/38	Negative	Negative		
3	9/ 9/38	Negative	Negative		
3	9/15/38	+	++		
4	9/20/38	++	+	++	
5	9/20/38	Anticomplementary	Negative		Negative
5	10/ 3/38	Positive	Negative		Negative
6	9/24/38	Specimen contaminated and unfit			

then sent to me for blood tests in a third laboratory and for examination and advice. I found no evidence of syphilis. The fact is notable that her mother, father, brother, sister and husband were all known to have negative Wassermann reactions. Her personal history and physical examination offered no hint of syphilis. Those conditions that are said to produce biologically false positive serologic reactions for syphilis were not present. The Wassermann and Kahn tests in the third laboratory gave negative results. Blood samples were sent to three nationally known laboratories. A complete summary of the various tests is given in the table.

The patient was advised to submit to a short course of antisyphilitic treatment. This she refused to do. On Feb 23, 1939 she was delivered of a 7½ pound (3,402 Gm) girl. The baby showed no abnormalities and has progressed normally since birth. The results of Kahn and Wassermann tests on March 9 were reported "doubtful" for the mother and negative for the father and baby.

From the Section on Dermatology, Lois Grunow Memorial Clinic

Clinical Notes

PURPURA DUE TO INJECTION OF ESTROGENIC SUBSTANCE

EARL L. LOFTIS, M D, DALLAS, TEXAS

After a fairly thorough search of the literature I failed to find a report of a reaction to estrogenic substance similar to that of a patient I have under observation. Therefore, I believe her case will be of interest.

REPORT OF A CASE

Mrs I N, aged 44, consulted me three years ago for treatment of eczema limited to the forehead and purpura limited chiefly to the thighs. The latter lesions were bluish purple and varied in size from that of a dime to that of a 25 cent piece. The eruption had been present several days, and some of the lesions were fading and new ones were appearing. Close questioning revealed a history of weekly injections of an estrogenic substance. The dermatitis of the forehead proved to be of the contact type. The injections of estrogen were stopped for three weeks, and all the lesions disappeared except the faint outline of one of them. The injections were resumed and within twenty-four hours numerous lesions again appeared on the thighs. One of the lesions was fixed, fading slowly and leaving a permanent faint trace. Bleeding of the gums always accompanied the attacks. Repeated tests were made at intervals, with different doses of the estrogenic substance and with different vehicles. The result was always the same. Aqueous and oily solutions caused the same reaction, proving that the vehicle was not responsible for the eruption. Physical examination and laboratory tests, including complete studies of the blood, made when the eruption was present and also between attacks, have given negative results except for a basal metabolic rate of —16 per cent.

1502 Medical Arts Building

CHEILITIS AND DERMATITIS FROM RESORCINOL AND A DERIVATIVE

H J TEMPLETON, M D, OAKLAND, CALIF

In 1932 I reported,¹ along with Lunsford, a series of cases of cheilitis and stomatitis from a toothpaste containing hexylresorcinol. Since then I have observed additional cases in which this condition was caused by the same toothpaste or by a mouth wash containing the drug. There have also been reports in the literature of dermatitis from resorcinol used in hair tonics and in rectal suppositories. I recently saw a patient who is sensitive both to resorcinol, which she used in a hair tonic, and to its derivative hexylresorcinol, which she used in

¹ Templeton, H J, and Lunsford, C J. Cheilitis and Stomatitis from ST37 Toothpaste, Arch Dermat & Syph 25 439-443 (March) 1932

lozenge form This patient came to me complaining of dermatitis of the ears and also of cheilitis and stomatitis Her history and a strongly positive result of a patch test indicated that the dermatitis of the ears was caused by a hair tonic I had given her which contained 5 per cent resorcinol in alcohol The stomatitis was apparently caused by lozenges containing hexylresorcinol ("sucrets"), as evidenced by a strongly positive reaction to a patch test with one of the lozenges Moreover, she recalled that she had had a similar attack of stomatitis on a previous occasion when she had sucked a lozenge of the same brand. The first attack of stomatitis was prior to the use of the hair tonic

Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

LYMPHOBLASTOMA IN MICE FOLLOWING ADMINISTRATION OF CARCINOGENIC TAR AUSTIN M BRUES and BEULA B MARBLE, Am J Cancer 37 45 (Sept) 1939

In a strain of mice normally exhibiting a 2 per cent incidence of lymphomatosis and a subleukemic blood picture it was observed that lymphoblastoma or lymphatic leukemia developed in 50 per cent of them after the cutaneous application of three different fractions of carcinogenic tars for a prolonged period. The lesions likewise showed a rapid course, whereas the spontaneously appearing lesions were chronic. It was concluded that in the presence of a latent predisposition to lymphoblastoma a carcinogenic agent may act as an extrinsic precipitating factor.

AN EVALUATION OF THE RISK OF BIOPSY IN SQUAMOUS CELL CARCINOMA RALSTON PATERSON and JOHN R NUTTALL, Am J Cancer 37 64 (Sept) 1939

In a carefully controlled and specially selected group of 166 patients, biopsy specimens were taken from 99 with a sharp ring forceps. The time between the original investigation and treatment and the analysis of the end results varied from one and one-half to four and one-half years, and the lesions studied were from the oral mucous membrane and from the skin. The incidence of metastases was not increased in those histologically studied.

FOERSTER, Milwaukee

TORULOSIS INVOLVING THE HUMAN CEREBRUM W E ROBERTSON, H F ROBERTSON, H RIGGS and L SCHWARTZ, J A M A 113 482 (Aug 5) 1939

A physician aged 61 suffered for four years with attacks of dizziness, syncope, dimness of vision, photophobia and increasing muscular weakness. At times there was incontinence of feces and urine. He experienced increasing memory failure and ultimately complete disorientation. There were hyperreflexia, arteriosclerosis of the fundi and peripheral arteries, tremor of the hands and tongue and muscular atrophy. The eyes showed vertical nystagmoid movements. The leukocytes numbered 17,000 per cubic millimeter, with 92 per cent polymorphonuclear cells. The spinal fluid was not under increased pressure and contained 123 cells per cubic millimeter, of which 50 per cent were polymorphonuclear leukocytes, 44 per cent were lymphocytes and 6 per cent were endothelial cells. Histologic examination of a specimen of muscle ruled out myasthenia gravis. The correct diagnosis was not surmised until the study of postmortem material revealed the organism infiltrating into brain tissue. Part of the symptoms were considered due to the effect of the infection on the cerebral circulation.

HISTOPLASMOSIS OF DARLING F J SHAFFER, J F SHAUL and R H MITCHELL, J A M A 113 484 (Aug 5) 1939

A white girl aged 11 months was observed by Shaffer, Shaul and Mitchell because of intermittent fever and vomiting of six months' duration and drowsiness and alternating diarrhea and constipation of one month's duration. The child was suffering with malnutrition and had a rectal temperature of 103.2 F. There was bilateral cervical adenopathy and scaling of the hands and feet. The spleen extended down to the iliac crest, and the liver was palpable 6 cm below the costal margin. Several tumefactions of purpuric appearance developed and ulcerated. There were leukopenia and anisocytosis. The diagnosis was not established before death. Parasitic bodies were seen in sections of the skin, liver, spleen, pancreas,

intestine, mesenteric lymph nodes, adrenals and bone marrow The organisms were observed almost without exception in large endothelial cells By means of the oil immersion technic, each body was found to consist of a central portion surrounded by a capsule The organism *Histoplasma capsulatum* was differentiated from Donovan bodies by the irregularity of its chromatin nucleus and because it did not possess a rod The authors stated that this case of histoplasmosis is the fourth to be reported in the United States and the eighth in medical literature

DERMATITIS OF THE EAR H L WILLIAMS, H MONTGOMERY and W N POWELL,
J A M A **113**:641 (Aug 19) 1939

In a clinical and laboratory study of 25 patients who exhibited eczematous lesions of the external ear, Williams, Montgomery and Powell were unable to establish definitely in any case that the dermatitis was primarily due to a bacteria, fungi or allergy The pathologic changes observed in 7 of the cases were not diagnostic, they were features suggestive of contact and atopic eczema and of localized neurodermatitis in varying degrees The bacteriologic observations showed a variety of micro-organisms in the different patients In 18 of the 25 cases careful removal of detritus and cleansing the external auditory canal were the most important factors in clearing up the dermatitis No single drug was considered of specific importance, but if a variety of drugs is available, hypersensitive reactions may be avoided, and treatment is usually effective

A CASE OF PURPURA HAEMORRHAGICA RESULTING FROM SEDORMID H H HUBER,
J A M A **113**:674 (Aug 19) 1939

Huber reported the case of a physician in whom systemic reactions and hemorrhagic sequelae developed on two occasions after the ingestion of sedormid (allylisopropylacetylcarbamide) The symptoms began two hours after taking the drug, with a severe chill, followed by fever and later by nausea, vomiting, vertigo and the development of purpuric lesions During the second attack hemorrhage occurred from the mouth, and the purpuric lesions were numerous Laboratory tests revealed low platelet counts (dropping to 20,000 per cubic millimeter), a positive result to a capillary fragility test and a bleeding time of over ten minutes A return to normal conditions followed soon after a blood transfusion

OCCUPATIONAL LEUKODERMA PRELIMINARY REPORT E A OLIVER, L SCHWARTZ
and L H WARREN, J A M A **113**:927 (Sept 2) 1939

Oliver, Schwartz and Warren report the development of leukoderma in workers who used a particular brand of rubber gloves The patches of leukoderma occurred on skin under the gloves and in certain instances on covered portions of the body Patch tests with the chemicals in the gloves showed that an antioxidant caused positive reactions in all the affected workers, and later depigmentation occurred The trade name of the antioxidant was agerite alba and was said by officials of the company at which the gloves were manufactured to be monobenzyl ether of hydroquinone containing less than 1 per cent of unchanged hydroquinone When the workers ceased wearing the gloves with the antioxidant, some return of pigment was noted

EXPERIMENTAL AND CLINICAL GRANULOMA INGUINALE R B GREENBLATT, R B
DIENST, E R PUND and R TORPIN, J A M A **113** 1109 (Sept 16) 1939

Greenblatt, Dienst, Pund and Torpin coin the word "pseudobubo" to describe the inguinal swelling of granuloma inguinale which they found to simulate the bubo of other venereal diseases Histologically, the pseudobubo shows the structure of a subcutaneous granuloma Regional lymph nodes, which were excised and studied microscopically in 4 cases, frequently showed endothelial cells containing Donovan bodies This showed that the infection may travel by way of

the lymphatics The condition was experimentally reproduced in 3 human beings and failed to develop in 1 The disease was at its height in about fifty days after inoculation, but the exact incubation period was not determined The authors failed in attempts to inoculate laboratory animals and were unable to verify the work of others who had previously reported success in culturing Donovan bodies

INFECTIOUS RELAPSE IN SYPHILIS OF MORE THAN TWO YEARS' DURATION
H PARISER, J A M A 113 1206 (Sept 23) 1939

Pariser reexamined a group of 120 patients who had previously received treatment for primary or secondary syphilis and whose infection was of at least two years' duration He discovered 6 instances of infectious relapse, an incidence of 5 per cent In 2 of the 6 cases treatment was begun while they were in the primary stage of the disease, with positive serologic reactions In 4 cases there was a tendency toward early serologic reversal, in 2 of these there was a tendency toward relapse in serologic reactions While irregularity of treatment is a contributing factor of importance, Pariser states that one is forced to conclude that there exists a small refractory group of patients who in spite of adequate therapy may exhibit infectious relapse

MASSIVE DOSE CHEMOTHERAPY OF EARLY SYPHILIS BY THE INTRAVENOUS DRIP METHOD H T HYMAN, L CHARGIN, J L RICE and W LEIFER, J A M A 113 1208 (Sept 23) 1939

Hyman, Chargin, Rice and Leifer report on the results of treatment in a series of 86 men with primary or early secondary syphilis The technic of medication followed that used in a preliminary series The patients were hospitalized, and neoarsphenamine was administered by the intravenous drip method, the average total dose being in excess of 41 Gm The average duration of treatment was slightly less than five days The results confirm those obtained from the first series Spirochetes disappeared from the lesions within twenty-four hours, and a reversal of serologic reactions was obtained in 90 per cent of the cases There were 4 admitted failures, 2 clinical relapses and 2 relapses in serologic reactions There was 1 death, which was due to hemorrhagic encephalitis Forty-nine patients (57 per cent) experienced fever early in the course of treatment, and in 54 patients (63 per cent) fever was noted toward the latter part of therapy Eruptions of scarlatiniform or morbilliform character or simulating erythema multiforme occurred in 42 patients (52 per cent) There was 1 instance of dermatitis exfoliativa Peripheral neuritis occurred in 31 patients (38 per cent), developing two to three weeks after their discharge from the hospital and lasting as long as four to six months In 4 patients there developed mild jaundice An elevated icterus index was noted in 12 patients, but in no instance was there any clinical evidence of hepatic damage No evidence was found of renal irritation or damage Besides the fatal case of hemorrhagic encephalitis, 1 patient exhibited a single convulsion, without further symptoms Nitritoid crises, the various types of atrophy and degeneration of the liver, aplastic anemia and pulmonary embolisms were not present in any case Approximately 60 per cent of the total administered dose of arsenic was recovered from the urine and feces in 12 unselected cases

Lewis, New York

CUTANEOUS SENSITIZATION STUDIES II GROSS AND MICROSCOPIC CHANGES IN RAGWEED AND 2-4 DINITROCHLOROBENZENE SENSITIZATION OF GUINEA PIGS, AND IN POISON IVY SENSITIZATIONS OF HUMAN BEINGS JULIUS E GINSBERG, C DUNCAN STEWART and S WILLIAM BECKER, J Invest Dermat 2 81 (June) 1939

The work of Brunsting and Bailey is repeated in producing cutaneous sensitization to ether extract of short ragweed pollen in guinea pigs through topical applica-

tion of the substance. It is further observed that by continuing to paint the skin of the sensitized pigs, they become desensitized. The analogy of this phenomenon to the "hardening" of the skin of human beings in industry is pointed out. It was found that animals previously sensitized to horse serum showed no greater tendency to become subsequently sensitized to ragweed than did those not so sensitized.

Some of the studies made by Landsteiner and Jacobs on the sensitization of animals with simple chemical compounds were also repeated. Animals sensitized to 2, 4-dinitrochlorobenzene by surface application attained the same degree of sensitization as those sensitized by intracutaneous injection of the same substance. Animals sensitized to this chemical showed no greater tendency to become subsequently sensitized to ragweed than did previously unsensitized or horse serum-sensitized animals.

Histologic study of these eczematoid lesions in the guinea pig showed many similarities to those of the human skin. However, there were striking differences, accounted for on the basis of differences in the degree of reaction and on the known differences between human and animal skins.

DAVIS, Nashville, Tenn

ECZEMA MAMMARUM SYMMETRICUM ROMAN LESZCZYNSKI, Brit J Dermat
51:301 (July) 1939

In all of 20 cases of eczema of the nipples and areolas in women the author has also observed dysmenorrhea, that term being used to signify menstrual disturbances in general. This projection onto the mammary skin of an upset in the hormonal or neurovegetative system may be a sensory or trophic reflex which provokes itching and then inflammatory changes. In addition to giving local treatment it is necessary to direct therapy against hormonal disturbances and inflammatory diseases of the genital organs.

THE GLOMUS TUMOR DOUBTS AND DIFFICULTIES IN DIAGNOSIS J H TWISTON
DAVIES, F F HELLIER and ROBERT KLABER, Brit J Dermat 51:312 (July)
1939

A group of 6 cases is reported in each of which there were reasons for considering a diagnosis of glomus tumor. Masson has described three varieties of glomus tumor: angiomatous, epithelioid (paucivascular) and neuromatous. In addition he has described a "tumeur angio-myome arteriel" and stated the belief that it originates from the glomus. The lesion in 1 of the 6 cases seemed to correspond with this type, and in another it was an example of Recklinghausen's disease with tender angiomatous nodules. In 1 case the lesion was thought to be a heterotopic glomus on the back of the thigh, a site in which the glomus does not normally occur in man. In only 2 of the cases were there typical glomus tumors. The histologic observations are described and illustrated with photomicrographs.

CLASSIFICATION AND DEFINITION OF THE CLINICAL VARIETIES OF ERYTHEMATODES
(LUPUS ERYTHEMATOSUS) WITH PARTICULAR REFERENCE TO ITS ACUTE AND
SUBACUTE COURSE ERICH URBACH and CARMEN C THOMAS, Brit J Dermat
51:343 (Aug-Sept) 1939

Urbach and Thomas propose a classification of erythematodes (a name which they prefer to lupus erythematosus) that distinguishes chronic, exacerbated and acute forms for both the disseminated and the discoid variety, with a subdivision further into acute and subacute, depending on the duration of the disease. The discoid lesions are characterized by peripheral extension of the borders, and the disseminated ones, by an increase in the number of lesions, rather than by their peripheral growth. With case histories they illustrate the following types of the

disease (1) chronic discoid, (2) chronic disseminated, (3) exacerbated discoid, both acute and subacute, (4) exacerbated forms of disseminated, both acute and subacute, and (5) acute and subacute forms, depending on duration and constituting the conditions which begin abruptly, without any preceding lesions

The authors recognize the fact that there may be conditions which overlap and will not permit precise classification. In cases in which there is hypersensitiveness to light and no porphyrin is recovered in the urine or blood, it is suggested that the feces be investigated

THE USE OF SULPHANILAMIDE IN STREPTOCOCCIC DERMATOSES JAMES M FLOOD and JOHN H STOKES, *Brit J Dermat* 51 359 (Aug-Sept) 1939

A group of 6 cases is presented of incapacitating cutaneous eruptions of polyvalent causation, in which hemolytic streptococci played an important role and which with the use of sulfanilamide were brought under control. The conditions were sycosis, dyshidrotic eruptions with secondary infection and various postular dermatoses. After the eruptions were brought under control by sulfanilamide, other treatment was instituted, depending on the cause of the disease

PERIADENTITIS MUCOSA NECROTICA RECURRENS (SUTTON), ULCUS NEUROTICUM MUCOSA ORIS (LOBLOWITZ) A GIRDWOOD FERGUSON, *Brit J Dermat* 51 366 (Aug-Sept) 1939

Ferguson records a case in which a girl aged 17 had had the disease for five years. The histologic examination showed a nonspecific granuloma, with central necrosis. The literature on the subject is brought down to date

INFECTION OF A PEACOCK WITH ERYSIPELOTHRIX RHUSIOPATHIAE, FOLLOWED BY A CASE OF HUMAN ERYSIPELOID AVERIL W GREENER, *Brit J Dermat* 51 372 (Aug-Sept) 1939

A case is described in which erysipeloid appeared on the hand of an attendant who handled the carcass of a peacock infected with *Erysipelothrix rhusiopathiae*

GOWERS' CASE OF LOCAL PANATROPHY STANLEY BARNES, *Brit J Dermat* 51 377 (Aug-Sept) 1939

The main features of the case were the occurrence of patches in the skin of morphea-like atrophy of irregular distribution and shape. There was no evidence of excessive fibrous tissue in the skin, subcutaneous tissue or muscle, and the

from others described in the literature in that in them there is usually a sclerotic element or a diffuse progressive lipodystrophy. In others the atrophy is diffuse, affects large areas and leaves the muscles unaffected

CHLOR-ACNE IN RAILWAY WORKERS H HALDIN DAVIS, *Brit J Dermat* 51 380 (Aug-Sept) 1939

An outbreak of chlor-acne in a group of railway workers is reported. The peculiar feature was that only men that worked indoors were affected. They were employed in pulling wire covered with chlorinated naphthalene through conduits which were above their heads. Apparently they were affected when particles of the coating fell on their heads, necks and forearms, for other men engaged in the same work outdoors were not affected. It is thought that outdoors the particles of dust were blown away

RATTNER, Chicago

NODULAR CIRCUMSCRIBED GIANT LICHENIFICATION OF THE SCROTUM A TOURAINE and E LORTAT-JACOB, Bull Soc franç de dermat et syph 46:695 (April) 1939

The patient, a man aged 42, presented himself for treatment of giant circumscribed lichenification of about a year's duration. There was intense pruritus. On the left side of the scrotum were two large pseudotumors, measuring 30 by 25 cm and 40 by 25 cm. Under general anesthesia the lesions were excised. Healing was uneventful, and the result was entirely satisfactory, the pruritus being completely relieved.

PRELIMINARY NOTE ON THE USE OF VITAMIN P-P IN THE TREATMENT OF SEBORRHEA AND ACNE A DESAUX, R GOIFFON and H PRÉTET, Bull Soc franç de dermat et syph 46:715 (April) 1939

The authors mention that nicotinic acid seems to influence porphyrin metabolism. They report on acne and seborrhea in 2 young girls, which improved considerably after the administration of nicotinic acid. They merely suggest that their observations encourage further trial of such therapy.

LUPUS ERYTHEMATOSUS L M PAUTRIER, Bull Soc franç de dermat et syph 46:966 (Sept-Oct) 1939

Pautrier recalls that in 1903 he championed the theory that lupus erythematosus is due to the tubercle bacillus. He comments that in the cases in which postmortem examination failed to reveal tuberculosis he always found that some organ had escaped the anatomicopathologic examination necessary for the proof.

Pautrier mentions that in 1926 he expressed his belief that the filtrable forms of the tubercle bacillus plays a role in various so-called tuberculids. He admits, however, that the rarity of positive results of inoculation experiments in lupus erythematosus are discouraging to those who believe in the tuberculous cause, especially in view of the frequency of lupus erythematosus. Even tuberculoid structure is not found, which emphasizes the difficulty in proving that lupus erythematosus is due to the ordinary form of the tubercle bacillus.

He believes that cutaneous tuberculosis must exist in two forms, one due to virulent tubercle bacilli (ordinary type) and the other due to an avirulent or weakly virulent filtrable type, the latter possibly rendered avirulent by the skin itself.

Pautrier also cites Lowenstein's positive results in the blood culture of the tubercle bacillus, admitting, however, that the negative results of other workers were discordant. Pautrier states the belief that some authors in speaking of blood cultures refer to the tubercle bacillus in its classic form, which on culture gives rise to "macrocultures," visible to the naked eye, while others speak of "microcultures," discernible only by scraping the culture plates and staining the debris by the Ziehl method. Certain observers have stated the opinion that organisms forming this type of culture represent the tuberculosis ultravirus, weakly virulent and possessing a low "allergizing" power. The form in which the bacillus circulates in the blood seems to be this young type, giving rise to ultravirusemia. Pautrier believes that the filtrable form of the tubercle bacillus at least offers a good hypothesis as to the causation of lupus erythematosus.

CRITERIA FOR DIAGNOSIS OF LUPUS ERYTHEMATOSUS H GOUGEROT, Bull Soc franç de dermat. et syph 46:971 (Sept-Oct) 1939

According to Brocq, Besnier and Darier the three main clinical criteria for the diagnosis of lupus erythematosus are erythema, hyperkeratosis (especially follicular) and cicatricial atrophy.

Histologic criteria, as given by Civatte in accordance with Gans, are follicular hyperkeratosis, epidermal atrophy, vascular dilatation, edema of the papillary

body and lymphocytic infiltration, with partial conservation of the elastic tissue in the infiltrate. Civatte also adds lymphocytic exocytosis ordinarily without spongiosis in the epidermis.

Gougerot states the belief that the disease is tuberculous. In 1906 he obtained positive results in 2 cases after inoculation into monkeys. He feels that for successful results large pieces of skin must be used and not merely the fragments obtained during removal of a specimen for biopsy. He cites other observers who have obtained similar successful results (Ehrmann and Reines, Bloch and Fuchs, Cannon and Ornstein, Nicolau and others) and maintains that the efficacy of gold therapy is a point in favor of the theory that lupus erythematosus is a tuberculous disease.

LAYMON, Minneapolis

STRUMOUS BUBO OF TUBERCULOUS AND LYMPHOGRANULOMATOUS ORIGIN N MELZER and K SIPOS, *Acta dermat-venereol* 20 135 (March) 1939

The authors cite a case of a woman presenting a swelling in the inguinal region of one year's duration. The Frei test gave a positive reaction. Pus obtained by puncture was injected into the peritoneal cavity of guinea pigs, in which generalized tuberculosis developed. The patient gave a positive reaction to a Frei antigen made of her own pus (from the bubo). Positive reactions to the same antigen were obtained in 2 other patients suffering from lymphogranuloma. The authors stated the belief that this strumous (scrofulous) bubo was caused by a mixed tuberculous and lymphogranulomatous infection.

CHRONIC LOCALIZED INFLAMMATION CHARACTERIZED BY LYMPHADENOID STRUCTURE W L L CAROL and J R PRAKKEN, *Acta dermat-venereol* 20.147 (March) 1939

The authors describe 4 cases of lymphocytomas located, respectively, on the nose, cheeks, ears and labia minora. The histologic picture showed granulation tissue with predominance of lymphocytes.

The literature is reviewed, the clinical manifestations of this entity are described, and the differential diagnosis is considered.

FIVE CASES OF LYMPHOGRANULOMA INGUINALE IN CHILDREN C E SONCK, *Acta dermat-venereol* 20 171 (March) 1939

The author describes 5 cases of lymphogranuloma venereum in children whose parents also suffered from the same disease. The girls belonged to three different families, and 3 of them were sisters. Most of the patients and their mothers presented involvement of the rectum with strictures. Three girls also had hydrarthroses of the knee joints. The picture of the disease and the course of the infection in small girls does not seem to show any essential difference from that in women. The parents acquired the infection only after all the children were born, which excludes the possibility of the disease's being inherited by the children.

These cases prove that lymphogranuloma venereum can be transmitted not only through sexual intercourse but also in other ways.

TREATMENT OF OCCUPATIONAL DERMATITIS WITH VITAMIN A AND D I DAINOW, *Acta dermat-venereol* 20 191 (March) 1939

The author describes patients treated with intramuscular injections of vitamins A and D (he used a solution containing 10,000 U S P units of each vitamin in each cubic centimeter). The cutaneous manifestations disappeared, and a real desensitization was obtained. Some of the patients returned to their work soon,

others were treated and cured without having to stop work. The author believes that vitamins A and D exist in the normal skin and that their content in skin varies according to the state of bodily deficiency.

ETIOLOGY OF AURICULAR APPENDAGES T BRANDER, *Acta dermat-venereol* 20.213 (May) 1939

The author describes a case of a 3 month old girl with bilateral auricular appendages. Her mother and 1 uncle (mother's brother) had the same condition unilaterally. Two other children of the same parents were normal, while a brother of the patient presented the same malformation. Cases are reported in which this condition appeared in only 1 of twins. The author, however, claims to have enough data on families with frequent appearance of auricular appendages to prove to himself beyond doubt that heredity is a decisive factor in the occurrence of these malformations.

SOME PROBLEMS CONCERNING THE PATHOGENESIS OF ALLERGIC ECZEMAS, ELUCIDATED BY EXPERIMENTS ON SENSITIZATION WITH DINITROCHLOROBENZENE H HAXTHAUSEN, *Acta dermat-venereol* 20.257 (May) 1939

Haxthausen produced a generalized hypersensitivity to 1 per cent solution of dinitrochlorobenzene, by painting a small area of skin once with a 30 per cent solution of dinitrochlorobenzene in acetone. A hematogenous spreading of the hypersensitivity is considered possible, because it appeared on islands of skin isolated from the surrounding skin by means of incisions and with the same intensity as outside the islands. That the epithelial cells are of some importance in the process of sensitization is proved by the fact that freezing with solid carbon dioxide immediately or one to eight days after the painting prevented hypersensitivity in about 80 per cent of the cases. Ultraviolet irradiation one day before the application of the sensitizing solution did not prevent the appearance of hypersensitivity.

PRIMARY TUBERCULOUS INFECTION OF THE SKIN AND MUCOUS MEMBRANE SVEN HELLERSTROM, *Acta dermat-venereol* 20.276 (May) 1939

The author describes 2 cases of primary tuberculous infection. In a young girl an ulceration on the vulva and inguinal adenitis developed a few weeks after sexual intercourse with a man who had definite tuberculosis of the genitourinary tract. Histologic examination of the ulceration and the lymph gland proved these lesions to be of tuberculous character. The second case was that of a man on whose nose there developed an excoriation due to an accident in a swimming pool. Six weeks later numerous characteristic lupus nodules appeared around the site of the abrasion. The results of histologic examination of a nodule confirmed the diagnosis of tuberculosis.

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BROOKLYN DERMATOLOGICAL SOCIETY

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November-December 1939

Diffuse Pigmentation, Incontinentia Pigmentia Presented by DR JACOB SKEER

H P, a girl aged 14, born in the United States, consulted me because of a generalized pigmentation of four years' duration. The patient stated that it first appeared after sunburn. Both parents are alive and well, and she has a sister, 16 years old, also in good health. As a child she had chickenpox, whooping cough and measles. She complained of headaches about five years ago, but they disappeared after she began to wear glasses. She graduated from elementary school at the age of 13. She began to menstruate at the age of 12 years. Her periods are regular, of six days' duration, with pain the first day.

Physical examination shows that her hair is streaked with numerous gray hairs and that there is slight pityriasis of the scalp. She has a high forehead, prominent bosses and a wide space between her eyes, which are of a mongoloid type. There are numerous pinhead-sized milia on the margins of the upper and lower eyelids and on the malar regions. The posterior cervical glands are somewhat enlarged.

Examination of the skin shows that on the forehead, beginning from the temple region and extending toward the middle, there are irregular, reticulated, blotchy areas of pigmentation, beginning at the hair line and extending to about $\frac{3}{4}$ inch (1.3 cm) above the eyebrows. The pigmentation branches out and becomes less in the midline. There are a few spots on the malar and mandibular regions and anterior to the ears. The skin of the arms is also involved, especially the external aspect, where there are numerous large patches with many branches, terminating in points in clawlike arrangement, forming irregular circles and segments like the veins of marble. The flexor surfaces and the interior aspects of the arms, as well as the palms, are free of lesions. There are two irregular linear patches in the anterior axillary line. On the back there is a patch over each scapula, with numerous filaments branching out and forming finer projections, terminating abruptly in points. On the extensor surface of both thighs, from the lower third to below the knees and extending on the tibial region of the legs and the calves, there are similar patches. There is decided dermatographism. All the finger nails have horizontal linear air spaces, with numerous striations, irregularities and pitting.

The Wassermann reaction of the blood was negative.

Histologic examination showed a positive dopa reaction in the epidermis and only an occasional cell in the corium. Sections stained with hematoxylin and eosin showed that the epidermis and the cutis were practically normal. There were occasional cells containing brownish pigment about the blood vessels and in the corium.

DISCUSSION

DR LESSER M FRUCHTBAUM. I wonder if this entity should be classified among the nevi. The distribution is in favor of it, and I think that perhaps the histologic examination will confirm this diagnosis.

DR ABRAHAM WALZER I think that the clinical description given for incontinentia pigmentia fits well in this case. The picture is that of a bizarre arrangement of irregularly shaped patches of tan pigmentation, with all kinds of peculiarly shaped borders. The final diagnosis rests, I think, on the histologic picture.

DR JACOB SKEER Incontinentia pigmentia is a rare cutaneous condition. A study of the histologic sections should give the diagnosis. This condition is supposed to be a congenital ectodermal anomaly which begins in intrauterine life. The anomaly of the ectoderm is often associated with changes of the nails, hair and bones of the skull. The histologic changes chiefly concern melanin. Melanin is found not only in the epidermis but in the cutis, and it is explained by the fact that the basal cells apparently cannot handle the amount of pigment that is formed and it therefore drips into the cutis, producing a sort of tattooing.

Lymphangioma Circumscriptum, Simple and Cavernous Presented by Dr E A GAUVAIN

S B, a boy aged 28 months, is presented from the Methodist Episcopal Hospital. A lesion had been present on the back of the neck for one year. It began as minute, white blisters in an area the size of a nickel. Later some subcutaneous swelling was noted just cephalad to the cutaneous lesion. The swelling increased rapidly to the size of a walnut during the two weeks before presentation.

There is a small group of tense, white or opalescent, pea-sized lesions on the back of the neck, just to the right of the cervical vertebrae. Immediately cephalad to this is a subcutaneous mass the size of a walnut that appears like a lipoma. It is, however, more tense and feels cystic. This tumor mass can be transilluminated.

DISCUSSION

DR E A GAUVAIN I was interested in the case from the standpoint of the two types of lesions, the simple and the cavernous lesions. As regards treatment, I plan on surgical excision.

A pure angioma could not be transilluminated. The lesion lacks the color of an angioma. Those two points are sufficient to rule out that diagnosis.

Phenolphthalein Eruption Presented by DR ARTHUR M PERSKY

G K, a white man aged 69, born in Germany, has lived in the United States for forty-three years. His occupation is that of a bartender. In May 1939 the patient experienced a sudden chill (while walking), followed by an eruption, which he described as itching red patches, involving the entire body except the face. The eruption was diagnosed as "hives." The itching subsided, but in the areas where the red patches were there developed a pigmentation. This persisted until the present except for a few spots which have disappeared. There was no history of drug taking.

Over the lower part of the chest and abdomen are scattered areas, ranging in size from that of a quarter to that of a palm, of reticulated pigmentation enclosing whiter than normal, glistening skin. These areas appear to be atrophic.

DISCUSSION

DR ARTHUR M PERSKY I first saw the patient one week ago today, when he presented a flat pigmented reticulated lesion over the chest and abdomen, the center of the lesion was glistening white. At that time the impression was that the condition might be poikiloderma vasculare atrophicum. I performed a biopsy but was not satisfied with the report. Some physicians thought the condition might be a fixed drug eruption. There was brownish pigmentation at that time, and there was no question of any erythema. He was given three doses of phenolphthalein on three consecutive days and presented himself today with lesions

intensified The lesions are purplish, violaceous and edematous The condition is the most acute exacerbation of a fixed eruption due to phenolphthalein that I have observed

DR LESSER M FRUCHTBAUM I saw this patient four months ago when he presented himself at the Kings County Hospital and took care of him for three months The lesions were more violaceous then than they are tonight At that time there was no question that the condition was a phenolphthalein eruption The patient gave a history of having had a similar attack years ago, and the condition apparently was a fixed eruption There is no question in this case that it is a typical drug eruption During these three months the color of the lesions faded to practically pale brown

DR M EDWARD GOEBEL What is the usual length of time required for a phenolphthalein eruption to disappear after ingestion of the drug is stopped?

DR SEYMOUR H SILVERS I should like to ask whether any one can explain the peculiar color in a phenolphthalein eruption Has any work been published on this topic?

DR ABRAHAM WALZER While cases of multiple sensitivity to drugs are possible, one must also consider that a reaction following the ingestion of one drug may be reproduced nonspecifically by another drug and still that patient need not be sensitive to the second drug For example, supposing a patient has urticaria from aminopyrine and when that rash has practically subsided the patient takes acetylsalicylic acid The urticaria may return, not because he is sensitive to acetylsalicylic acid, but because the drug nonspecifically reproduces the eruption If the patient is given acetylsalicylic acid again a week or two after the original aminopyrine rash has gone, no reaction will occur

DR MORTIMER J CANTOR There is no question of the diagnosis in this case right now When I saw the patient originally, one week ago, without the flare-up, the condition looked brownish and reticulated, and, in fact, the white spots looked as though they might be atrophic One would never think the condition might be a fixed drug eruption, with the peculiar reticulation The usual type of fixed drug eruption is a discoid patch of pigmentation with infiltration I think the condition in this case is a rare type of phenolphthalein eruption, simulating poikiloderma

Erythema ab Igne Presented by DR M EDWARD GOEBEL

C B, a woman aged 40, states that about eighteen months ago she applied an ice bag to the right side of her face daily, a few hours a day, for several weeks, because of pain which was caused by a stone in the salivary gland While she was using the ice bag, the right side of the face became decidedly red and swollen The redness persisted, in spite of the fact that she stopped using the ice bag For the last six months this redness has been gradually disappearing

Examination shows slight atrophy of the skin over the right jaw and some telangiectasia, with a honeycombed brownish pigmentation

DISCUSSION

DR DAVID M DAVIDSON The eruption in this case consists of a single patch with definite atrophy, telangiectasia and pigmentation In view of the fact that the eruption is unilateral and not symmetric, as in cases of poikiloderma, and also, in view of the fact that the patient was exposed to roentgen rays for diagnostic purposes, I suggest the diagnosis of roentgen sequelae

DR JACOB SKEER I wonder if the patient applied any tar ointments plus the ice bags, because with all the symptoms that were explained in giving the picture of a roentgen dermatitis, namely, telangiectasia, atrophy and pigmentation, one could readily think of poikiloderma of Civatte The tissues of the face and chest

simulated an edematous scleroderma. One probably could make a diagnosis of poikiloderma with scleroderma.

DR DAVID L. SATENSTEIN. I think the diagnosis of poikiloderma is the only possible one to be considered here, for the reasons already given.

DR ABRAHAM WALZER. This condition is not poikiloderma, nor is it Riehl's melanosis. I would be more inclined to accept it as a reaction to cold applications, as this is not infrequently seen on the abdomen after applications of ice.

DR G. F. PRICE. Why isn't it possible to get a roentgen dermatitis from exposures at the dentist's office? The output of the x-ray machine may be increased without the dentist knowing about it. About two years ago I had a patient in private practice with a definite roentgen dermatitis from one roentgen ray exposure for an abscessed tooth at a dentist's office. She had a definite roentgen ray burn on the jaw about the size of a quarter.

DR M. EDWARD GOEBEL. I have seen this woman for the last two months, and it seems to me that the pigmentation is getting more prominent. In view of the fact that it is only on one side and that she had severe redness and swelling when she used the ice pack, I thought the condition was erythema ab igne in an unusual location. Erythema ab igne usually occurs on the abdomen or on the back. This patient is shown because of the unusual location. The term ab igne is used because of the lack of a better one. Atrophy and telangiectasia are also seen with heat and cold burns and sometimes simulate roentgen ray burns. Somehow I do not think that one single roentgen ray exposure for pictures would produce such decided atrophy of the skin or the sequelae that are seen here.

Elephantiasis Nostras. Presented by DR. MAX LERNER

I. H., a white man aged 30, has been under investigation at the clinic of dermatology and syphilology of the Beth Moses Hospital for about six months. He stated that he injured his left leg about sixteen years ago. An infection developed that incapacitated him for a month, and his left leg and foot became greatly swollen. The size of his left leg and foot has remained stationary.

About five years ago a fungous infection developed in both feet. He received treatment at several clinics.

When seen in August 1939, the patient had active dermatophytosis of both feet, especially the toes, where the eruption was verrucous. This cleared up with local wet dressings.

At present both feet show subsiding dermatophytosis. The left foot and leg are enlarged to about twice the size of the right. The enlargement is due to a solid type of edema, almost fibrotic to the touch. There is little pitting on pressure.

A roentgenogram of the left leg showed no pathologic changes in the bones. The Wassermann reaction was negative. The blood count, examination of the urine and Frei test gave normal results.

DISCUSSION

DR MORTIMER J. CANTOR. The patient has never been outside of New York. Elephantiasis nostras means that type due to a chronic low grade staphylococcic or streptococcic infection. The condition is more common on the face, there it is known as solid edema. This case falls in the same class. The patient has had no acute recurrences, no fever and no chills. The dermatophytosis which was active is now practically gone, with practically no effect on the elephantiasis.

DR SEYMOUR H. SILVERS. I treated a patient who had had recurrent acute attacks on the face, which left chronic lymphedema. During the acute stage, I prescribed sulfanilamide. When the acuteness subsided, I treated the patient with fractional doses of roentgen rays. The condition apparently has cleared under this protracted treatment.

Xanthoma Tuberosum Multiplex Presented by DR M EDWARD GOEBEL

F L, a seaman aged 59, stated that in 1933 he worked as a watchman and was exposed to the sun, as he did not wear his shirt. Within a short time he noticed a rash on the upper part of his back. The lesions had white tops, and the eruption was itchy. The itching was relieved by baths. However, the eruption persisted, and in 1936, in spite of negative Wassermann reactions, he received sixteen injections of a bismuth compound. The lesions gradually disappeared. In 1938 he underwent an appendectomy, and subsequent to this the eruption reappeared and has gradually become generalized and has persisted. There is no itching at this time.

Examination shows a generalized symmetric involvement of the body, from the neck down, consisting of papules which are discrete and which vary from purple to brown and from chamois colored to skin colored. Some of the papules have a shiny top, and some appear to be umbilicated, as in lichen planus. The liver and spleen are palpable.

The results of chemical examination of the blood were normal. The Wassermann reaction of the blood and the results of urinalysis were negative. The icterus index was 69. Microscopic examination of tissue showed evidence of xanthoma. A roentgenogram of the skull showed mottling of the skull bones, with a bridging across the sella turcica. The long bones were normal.

The patient is shown because of the resemblance of the papules to lichen planus. The diagnosis of xanthoma multiplex was made only after a complete study of the case.

DISCUSSION

DR JACOB SKEER: All that I could discern clinically was an eruption of lichen planus. I could not see anything clinically that looked like xanthoma tuberosum multiplex. Some of the lesions showed a yellowish tinge.

DR DAVID L. SATENSTEIN: A study of the slides corroborated the diagnosis of xanthoma.

DR MORTIMER J. CANTOR: Clinically, under the artificial light some of the lesions have a peculiar color, not that of lichen planus, but a good many of them have more than the usual papular appearance of lichen planus. They appear dome shaped. Of course this should be better seen in sunlight. They are more elevated and slightly yellowish. There are two to three such lesions on the ulnar aspect of the wrists that are conglomerations of these small xanthomatous masses, which give the clinical appearance of annular lichen planus. I do not know whether the condition should be called xanthoma tuberosum multiplex. It might be better to call it generalized xanthomatosis with peculiar lichenoid lesions.

DR ABRAHAM WALZER: This patient has typical lichen planus. He has the papules, arrangement, size, border, central depression and everything that goes with lichen planus. He also has lichen planus lesions of the lip.

Indolent Ulceration of the Leg Presented by DR ABRAHAM WALZER

H I, a man aged 19, first appeared at the dermatologic clinic of the Jewish Hospital about a month ago. Outside of a fracture of the skull at the age of 10 years, from which he completely recovered, there was nothing in his past history of any importance. There was no history of tuberculosis in his family. He has always lived in New York.

His present trouble began about a year ago, with an infection of the right palm which had been incised. This was followed by an infection of the left thigh and of the anal region. In May, six months ago, the first "abscess" appeared on the leg, which broke down and formed an ulcer. About three months ago the right leg became similarly involved. Gradually new lesions developed on both legs.

At present he shows about two dozen ulcerations on the legs, more on the left than on the right. The primary lesion is a small pustule, which somewhat

increases in size, breaks and, instead of healing, forms an ulcer which extends peripherally. Thus ulcers of various sizes, shapes and depths are formed, which are indolent and refuse to heal. The edges are irregular and somewhat undermined, some are rolled and have practically no surrounding erythema. The bases of the ulcers are either granular or necrotic. The inguinal glands are not enlarged.

A histologic section of tissue taken from the border showed chronic inflammatory changes. Cultures showed no mycologic organisms but streptococci, diplococci, bacilli and staphylococci. Physical examination, roentgenograms and examinations of the blood and urine showed no abnormalities.

DISCUSSION

DR LESSER M. FRUCHTBAUM: I, too, had a similar case. A boy voluntarily produced many lesions on his legs. This process went on for a year, until his legs were put in a removable light cast, and then the lesions cleared up. All the lesions in the case just presented are easily accessible. I think the phenomenon is artificially produced.

DR DAVID M. DAVIDSON: This case is one of extensive pyoderma, regardless of what other name one may wish to call it.

DR DAVID L. SATENSTEIN: I have observed hundreds of cases like this in the Orient. The condition is common there and usually follows insect bites. Lesions develop which suggest ecthyma and go on to form deep ulcers. Often they are covered by a gelatinous secretion and a thick crust, and when that is removed the lesion is larger than one would expect. The condition is usually due to an infection, but that does not make any difference as far as therapy goes. If the lesions were excised, new ones would appear, the same thing would happen if they were cauterized. I finally packed them with 10 per cent sodium chloride solution, and then the lesions cleared up. That made a poor soil for the organisms to grow. Pyoderma is just a name, and I doubt if the condition in this case is an artefact.

DR JACOB SKEER: I was able to follow the case. The new lesions began as small red papules, which quickly became pustular and broke down with necrosis and spread peripherally. They are not artefacts.

DR M. EDWARD GOEBEL: About two years ago I presented a case similar to this one. All the laboratory work showed nothing but staphylococci. More and more lesions developed, and finally there was involvement of the vascular system. Both the legs were amputated, but the patient died. I do not believe the condition is an artefact. I want to emphasize the seriousness of these conditions.

DR H. H. SAWICKY (by invitation): In Florida among the turpentine workers, where insect bites are common, such ulcerations are not infrequent. They are insect bites, are secondarily infected and are called pseudomycotic infections. Sulfanilamide has been used in these cases, with good results.

DR ABRAHAM WALZER: The process begins as a pustule and opens, but instead of healing it spreads, forming a round punched-out ulcer. This condition was described by Castellani (*ARCH. DERMAT. & SYPH.* 18:857 [Dec] 1928) under the heading of pseudomycosis. Hamilton (*South M. J.* 24:195, 1931) under the title of indolent leg ulcers described the same condition. Various types of organisms have been described, such as organisms resembling gonococci, hemolytic streptococci and others. Under a simple protective dressing of a modified paste, the condition has improved from 50 to 60 per cent.

Pityriasis Rubra Pilaris. Presented by DR ABRAHAM WALZER for DR IRVING N. HOLTZMAN.

T. H., a white married man aged 27, an upholsterer by occupation, presented himself at the dermatologic clinic of the Jewish Hospital on Dec. 11, 1939, with

an eruption of eight days' duration. He stated that on the morning of December 3 he awoke with a burning sensation of the skin of his face. Examination in a mirror disclosed a bright redness, with scaling of his entire face. He attributed this to a shaving cream which he had used for the first time the preceding night. However, three days later he noticed a similar redness and "tight feeling" of his hands. This was followed by the appearance of small red "pimples" on his arms, trunk and feet. There was no pruritus.

At present he shows a diffuse erythema of the face, with scaling over the forehead, eyelids and perioral region. This diffuse erythema extends down to the neck line and involves the entire circumference of the neck. Both hands to a point about 2 inches (5 cm) above the wrists (glovelike) are diffusely reddened, the skin thick and scaling. Pressure on the erythematous area reveals a yellowish discoloration. The arms, trunk and lower extremities present a papular eruption, the individual lesions are pinhead sized and erythematous, some flat topped and lichenoid in appearance and others grayish and conical. These papular lesions are follicular in distribution. On the trunk the lesions impart a grater sensation to touch. In some areas the papular lesions coalesce to form small elevated erythematous patches. The intergluteal area is the site of diffuse erythema surmounted by a coarse, slightly adherent scale.

Histologic examination showed hyperkeratosis, especially of follicular apertures, slight acanthosis, with intercellular edema of basal and spinocellular layers, slight dilatation of the blood vessels of the corium (subpapillary plexus), and no noticeable cellular infiltrate in the corium or around the blood vessels.

Patch tests with the shaving cream gave negative results.

DISCUSSION

DR JACOB SKLER. I think the condition has all the symptoms of an acute clearcut pityriasis rubra pilaris.

DR LESSER M. FRUCHTBAUM. I do not think the condition is as clearcut as was suggested. There are typical lichen planus papules on the body, in the mouth and on the penis. I believe this is lichen planus.

DR DAVID M. DAVIDSON. The clinical picture here is sufficiently clear to make the diagnosis of pityriasis rubra pilaris. The man presents diffuse hyperkeratosis of both palms and soles and a seborrhea-like eruption on the face. There are numerous keratotic papules at the hair follicles scattered over the body, which coalesce over the elbows, forming patches simulating psoriasis. In my opinion this case has all the features of pityriasis rubra pilaris.

DR L. J. FRANK. I agree with the diagnosis of pityriasis rubra pilaris.

DR SEYMOUR H. SILVERS. I agree that this case is one of pityriasis rubra pilaris. However, the patient does not show the follicular keratotic papules on the dorsum of the proximal phalanges.

DR IRVING N. HOLTZMAN (by invitation). The interesting thing about this case is the extreme suddenness with which the condition began. The patient first presented himself with a bright scaly erythema of the face and hands, and until he disrobed I thought he had a contact dermatitis. The papules first appeared on the arms, and there were also a few scattered ones on the sides of the chest which were red and soft. It was only in this last week that typical follicular papules have appeared.

A Case for Diagnosis (*Erythema Elevatum Diutinum*?) Presented by DR ABRAHAM WALZER

D. R., a clerk aged 39, is presented with an eruption on his face and neck of about four years' duration. There was no history of tuberculosis or other serious illness in the patient or his family.

The first lesions appeared on the back of the neck and behind both ears as itchy red spots, which increased in size and became elevated. They formed either

one patch or a group of nodules. They lasted about three to four months and disappeared, without leaving any marks. New nodules reappeared on other parts of the neck and face and regressed in the same manner.

At present he shows on the back of the neck a number of groups of elevated hard flat nodules, pea sized or a little larger, covered by a thin scale; on the left cheek near the nose is an erythematous slightly elevated round patch, about the size of a quarter, sharply outlined, with a fairly smooth surface and with some telangiectatic vessels running across. There is no suggestion that it might have been made up of a number of individual lesions. On the same cheek at the angle of the jaw is another lesion, semiannular in outline, showing more scaling than the other patch. On diascopic pressure, a faint pigmented area remains. There is no history of ingestion of drugs.

A complete physical examination, as well as examinations of the blood and urine, showed nothing abnormal. Histologic examination of tissue removed from the back of the neck about a year ago showed a subacute inflammatory process, with no features of anything definite.

DISCUSSION

DR DAVID M. DAVIDSON: Two forms of erythema elevatum diutinum have been described, the Bury type and the Hutchinson type. The first is supposed to appear over the knuckles in young children, usually girls, and the second type in older persons, predominantly men. However, I do not believe that the eruption in this case simulates any of the types of this disease. To my mind this case is one of lupus erythematosus. Lupus erythematosus which does not leave atrophy has been described, and it can be classified somewhere between the discoid and the acute type. In the future, this condition may become definitely discoid and leave atrophy.

DR M. DICKMAN: The lesions are telangiectatic on the surface, raised and well circumscribed and have no scales. I considered both lupus erythematosus and sarcoid but favor the diagnosis of sarcoid.

DR ABRAHAM WALZER: I put that diagnosis down with a question mark because it was the best diagnosis I could make. This disease is of four years' duration, and these lesions come and go. There is little scaling, no patent follicles or any projection of scales in them, and the histologic picture does not show the slightest evidence of lupus erythematosus. The lesions on the back of the neck are nodular and not the type usually seen in lupus erythematosus. There is no clinical or histologic destruction in those lesions. Therefore, I think one also has to question the diagnosis of lupus erythematosus, at least for the present. Regarding the diagnosis of sarcoid, here again one must think of the peculiar development of the lesions and the complete absence of a sarcoid structure. Regarding the question of erythema elevatum diutinum, many of the textbooks still include it under granuloma annulare. I think the condition in this case is the Hutchinson type of erythema elevatum diutinum.

Pseudoxanthoma Elasticum with Angioid Streaks of Retina Presented by DR SEYMOUR H. SILVERS

A D., an unmarried man aged 43, a resident of the United States for the past seventeen years, complains of generalized itching of two years' duration and of imperfect vision.

Examination shows a well developed man who presents a mild, moist, well defined red macerated eruption in the inguinal region, involving also part of the scrotum. On both sides of the neck, extending to the face and down to the clavicle, there are ill defined patches devoid of hair and having a velvety texture. The color ranges from light yellow to lilac. The follicular openings are evident. Definite papules cannot be felt. The left axilla shows a similar velvety patch about the size of a palm, also devoid of hair but grayish white. A similar patch is present in the right axilla.

A blood count gave normal results except for showing 9 per cent eosinophils. The urinalysis gave normal results. The Wassermann and Kline reactions were negative. Roentgenograms of the bones failed to show Paget's disease. The arteries of the legs showed decided calcification. The histologic examination of a section of skin showed typical pseudoxanthoma elasticum.

DISCUSSION

DR SEYMOUR H SILVERS Since four weeks ago the patient's vision has decreased a great deal. He is a cook and has lost his job because he cannot read the menu. Sometimes when he walks in the street he sees double, and objects appear to him distorted. New hemorrhages are constantly appearing in the eyegrounds.

DR LESSER M FRUCHTBAUM Is pseudoxanthoma elasticum always associated with ocular symptoms?

DR SEYMOUR H SILVERS In a great number of cases there are associated ocular symptoms. Extensive roentgenograms of the skull and long bones did not reveal anything abnormal in this patient.

Multiple Idiopathic Hemorrhagic Sarcoma (Kaposi) Presented by Dr C B LOCASIO for Dr E A GAUVAIN

W B, a white man aged 73, is presented from the Kings County Hospital. He states that he has had bluish red, slightly infiltrated plaques on the dorsa of both feet for twenty years. Five years ago he received twelve roentgen ray treatments during three weeks, without any evident improvement in the lesions. He has also had diabetes for twenty years and has recently been receiving 20 to 30 units of insulin daily.

On the lateral and dorsal aspects of both feet and extending up the outer side of the left leg are bluish red, slightly elevated plaques with sharp borders. There are also several pea-sized to dime-sized lesions of a similar nature on the legs. On the dorsum of the left foot, in the center of one of the plaques, is a pea-sized vascular tumor resembling a granuloma pyogenicum.

Examination of the blood showed 177 mg of sugar per hundred cubic centimeters, with no other abnormalities. Examination of the urine showed a 2 to 4 plus reaction for sugar and a faint trace of albumin. The histologic diagnosis was multiple idiopathic hemorrhagic sarcoma (Kaposi).

DISCUSSION

DR ARTHUR M PERSKY There is no question in my mind as far as the diagnosis is concerned, but the patient was brought here because after he was kept in bed for twenty-four hours the lesion blanched so considerably that the diagnosis of Kaposi's sarcoma could not be made. If the condition were Kaposi's sarcoma, would the lesion blanch when the leg is elevated?

DR DAVID M DAVIDSON Last year I presented before this society (*ARCH DERMAT & SYPH* 39 1081 [June] 1939) an old man with Kaposi's sarcoma who showed besides the more characteristic lesions on the legs, the same flat, almost nonelevated, red, violaceous patches as this patient presents tonight. The fact that the erythema becomes paler when the patient is lying down can be explained by the fact that the condition is here in the inflammatory-angiomatous stage, and while he is lying down the blood drains out of the vessels.

DR ARTHUR M PERSKY I might add that about one week ago the patient had a pea-sized granulomatous mass on the dorsum of the foot which was thought to be a pyogenic granuloma.

Lichen Planopilaris (Pringle) Presented by Dr LESSER M FRUCHTBAUM

H P, a man aged 56, presented himself on Nov 18, 1939, at the Unity Hospital, with a history of having had a rash on his body and scalp for four weeks. The Wassermann test performed during that period gave a negative reaction.

The patient presents a generalized, profuse, somewhat pruritic eruption over the anterior and posterior aspects of the entire trunk and on the anterior aspect of the upper portion of both thighs. A few lesions are also present on the upper extremities, the forehead and the vertex of the scalp. There are no lesions on the forearms or penis. On the trunk the lesions are a mixture of flat, polygonal, violaceous papules and conical papules surmounted by thorny spines.

DISCUSSION

DR DAVID M. DAVIDSON: As this patient presents lesions of lichen planus and lichen spinulosus on the body and lesions resembling pseudopelade on the scalp, I should say that this is a case of Little's disease. I believe that Feldman described the pathologic changes of these lesions, all of which are supposed to show the typical picture of lichen planus.

DR SEYMOUR H. SILVERS: This is a rare disease. I should like to hear from those who have had an opportunity to observe other similar cases.

DR LESSER M. FRUCHTBAUM: The atrophy on the scalp is not a result of these lesions but is due to a burn which involved the entire scalp and which was present before the development of the lesions. I made the diagnosis of lichen planopilaris owing to the coexistence of the two types of lesions. On the scalp the lesions are almost macular; on the rest of the body they are papular.

The picture has changed since one month ago. At that time the lesions on the scalp were violaceous, whereas now they are more brownish. Only a few typical lichen planus lesions are evident on the anterior aspect of the upper portion of the thighs. All the lesions have gradually developed into the flat-topped, shiny, polygonal papules of lichen planus. There is no atrophy of the skin.

A Case for Diagnosis (Dermatophytid?) Presented by DR LESSER M. FRUCHTBAUM

E. B., a man aged 55, presented himself at the Long Island College Hospital about a year ago, with a generalized eruption on the trunk. Prior to that he was hospitalized with the same condition for several months. The lesions first appeared on the forearms and then spread to the trunk and lower extremities. They arose in crops, remained for several weeks and then cleared up. At no time was he entirely free from lesions.

The lesions now are mostly discrete and round, with clearing centers and infiltrated borders, and are topped with scales. On the forearms and hands the lesions have the appearance of eczematous dermatitis.

Intradermal tests revealed sensitivity to house dust. Desensitization with house dust, however, did not clear up the condition. Laboratory tests, including biopsy, gave negative results.

DISCUSSION

DR M. EDWARD GOEBEL: This man was seen by me about two to three years ago. Prior to that he was also treated by Dr. Graham, and he also attended the clinic at the New York Post-Graduate Medical School and Hospital. He had a generalized eruption at the time, consisting of erythema, vesicles and crusting, which presented the appearance of a contact dermatitis. A similar diagnosis was made at the New York Post-Graduate Medical School and Hospital clinic and also by Dr. Graham. His condition when seen by me was so severe that he had to be hospitalized, and he remained in the hospital about three months. However, since that time he has had periods in which his skin was clear and periods in which a dermatitis occurred. Urticarial wheals were also associated with the dermatitis. Laboratory tests at the time, including blood counts, urinalyses and Wassermann tests of the blood, gave negative results. Microscopic study of the skin showed a dermatitis. The patient used only paper and pencil at work and did nothing at home to account for the dermatitis. The

rash is different now from what it was when first seen two or three years ago. This is the first time I have had an opportunity of seeing him in five months. The picture is now one of mycosis fungoides.

DR J C GRAHAM I saw this patient when his cutaneous lesions first began and at that time made the diagnosis of a contact dermatitis. However, I was unable to locate the causative factor. I agree with Dr Goebel's statements about him.

DR DAVID M DAVIDSON I do not believe that a dermatophytid ever produces such lesions. The condition might possibly be a toxic eruption due to some drug, but on account of the bizarre forms that these infiltrated patches produce, I am more inclined to suggest the diagnosis of mycosis fungoides.

DR L J FRANK To me the lesions looked round and infiltrated, and on the lower part of the body they seemed more like erythema multiforme lesions. There was central clearing but not the central clearing one sees in dermatophytids. The lesions were acute, those on the arms being slightly infiltrated. The condition in this case should be considered as a premycotic stage of mycosis fungoides but not one of dermatophytid.

DR H L FEIGENBAUM This is an unusual case, in that it presents certain features of many different types of cutaneous diseases. There are some psoriatic lesions, especially around the scalp and hair line on the back of the neck. There are also some plaques on the forearms that have a psoriatic appearance. On the posterior part of the thighs the configuration of the lesions and their color are those of erythema multiforme. There are no lesions suggestive of dermatophytid. I, too, should be inclined to call the case one of mycosis fungoides, in the early, or pretumor, stage.

DR ABRAHAM WALZER The first impression that one gets is that the case is one of mycosis fungoides, but the color is somewhat against that diagnosis, being too red. There is a peculiar configuration of the lesions, which are indurated and infiltrated. Furthermore, these lesions are evanescent. The condition cannot be a contact dermatitis because of the peculiar type of lesions. I believe that it might be toxic annular erythema with some edema. There is one other possibility and that is an annular edematous type of Duhring's disease, in which there are recurrent attacks of annular edematous erythema.

DR LESSER M FRUCHTBAUM It was interesting to hear all the diagnoses suggested—dermatitis venenata, mycosis fungoides, erythema multiforme and dermatophytid, which was my last diagnosis with a question mark. When the patient consulted me a year ago there were typical lesions of mycosis fungoides, not the type seen tonight but infiltrated lesions with raised borders and no scaling of any kind. The lesions would disappear and reappear. The eruption reappeared one month ago. Tonight the picture varies from the one presented two weeks ago. Up to that time several eczematous lesions were present on the neck, in the groins and on the dorsum of the hands that were typical of dermatophytosis, especially those in the groins.

This man suffers from intense itching. When the lesions clear up he is perfectly well, and when they reappear he goes through the various stages again. He does not present the clinical picture of mycosis fungoides. That diagnosis can also be excluded by the history. Several biopsies were performed, and none revealed the picture of mycosis fungoides. In connection with the possibility of erythema multiforme, I tried to locate the focus of infection, without success. The patient was sensitive to house dust by scratch test. There were numerous lesions on his toes which clinically looked like dermatophytosis, which suggested that the lesion was a dermatophytid.

Tuberculosis of the Skin Presented by Dr G F PRICE

J C, aged 8 years, born in this country, is presented from the dermatologic clinic of St. Mary's Hospital. He had pneumonia in December 1937, followed by an ulceration on the outer aspect of the right ankle, which took about eight

months to heal. He had pneumonia in December 1938, followed by an ulceration on the lower third of the left leg. Both areas healed with an atrophic scar, studded with islands of normal tissue.

The condition began about October 1 as an acute inflammatory process, simulating a cellulitis. A smaller lesion on the left thigh began at the same time but responded to ammoniated mercury ointment U. S. P. The present lesion rapidly grew to its present size and proceeded to break down, discharging a thin, pale watery purulent discharge in three different areas. The patient was put to bed and given a high caloric diet, and with the use of ammoniated mercury ointment and sterile petrolatum the two upper ulcers healed. The lower ulcer is still open but reduced to about one-third its actual size.

The Wassermann reactions in October and November 1939 were negative. The urine was normal. Examination of the blood showed 9,500 white blood cells and 4,630,000 red blood cells per cubic millimeter and 86 per cent hemoglobin, with a differential count of 74 per cent neutrophils, 1 per cent eosinophils and 25 per cent lymphocytes. A smear showed no organisms. A culture showed gram-negative bacilli. A subculture was not identified (probably a contaminant). Microscopic examination on November 30 showed tuberculosis of the skin.

MANHATTAN DERMATOLOGIC SOCIETY

GEORGE C. ANDREWS, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Dec 12, 1939

Cheilitis. Presented by DR. GEORGE M. LEWIS

G. B., a college student aged 25, is presented from the Skin and Cancer Units of the New York Post-Graduate Medical School and Hospital. Inflammation of his lower lip developed eight months ago. Investigation in California and in New York did not reveal any contact, such as with toothpaste or lipstick, which could account for the eruption. He had eleven fractional (75 r) exposures to unfiltered roentgen rays at weekly intervals, various types of local therapy and restricted diets, to eliminate possible food allergens. Cultures failed to demonstrate any pathogenic fungi.

The patient presents acute inflammation of the lower lip, with redness, vesiculation and profuse scaling. Many of the vesicles have ruptured. The upper lip is similarly involved but to a less severe degree. Palpation confirms the fact that the inflammation is superficial.

DISCUSSION

DR. DAVID L. SATENSTEIN: The causative agent might be sunlight. I have seen similar conditions occurring during the summer, especially in persons who go to the beach and expose themselves a good deal. They get this type of lesion, and it persists for a long time. Such conditions are difficult to clear up. I have a patient coming to the office now whose eruption began in the early part of the summer. She is a young girl who went to the beach to tan. Her lip became swollen, and the vesicle formed. Every time she gets in the wind her lip swells. I therefore suggest sunlight as a possible cause. As a test I would expose the patient to a small amount of ultraviolet radiation.

DR. HOWARD FOX: Cases of cheilitis exfoliativa have usually presented two difficulties for me. I have seldom been able to discover the causation, and I have rarely been able to get beneficial results from treatment. Cosmetics, dentifrices and sunlight play a part in some cases.

DR. ANTHONY C. CIPOLLARO: I should like to ask if the manifestation of neurodermatitis ever resemble cheilitis.

DR E WILLIAM ABRAMOWITZ The consensus among nutrition experts is that there is a deficiency of vitamin B in the diet of the general public. I suggest the administration of riboflavin, in view of its favorable action against cheilitis of obscure origin.

DR PAUL GROSS (by invitation) If contact dermatitis can be ruled out in this case, two other possibilities remain. One was mentioned by Dr Abramowitz. Yet I do not believe that the cheilitis of this patient fits in with the picture of riboflavin deficiency, as described by Sebrell and Butler. Notwithstanding, a therapeutic test with riboflavin seems justified. The other condition to be considered is that of an exfoliative cheilitis confined to the lower lip, which really is a precancerosis. Microscopic examination may show changes of the epidermis, suggesting the latter diagnosis.

DR MAX SCHEER I think in this case the causative factor is probably exposure to light. The condition began when the patient was in southern California, and it was always most intense when he resided in that region. Having once begun, the condition persisted.

DR GEORGE C ANDREWS If light sensitization were the important factor, one would not expect involvement of only the upper lip.

DR GEORGE M LEWIS This man's case has been thoroughly studied from the standpoint of cosmetics and all possible external sensitizers with the exception of light. He will be further studied for the possibility that vitamin B deficiency is responsible or that the condition is a form of neurodermatitis or a manifestation of neurasthenia. If precancerosis is a possibility, the question of a biopsy must be kept in mind. There is a history of seborrhea, but his scalp has been free of that disorder since he has been in New York.

Mycetoma Presented by **DR GEORGE M LEWIS** and **DR WILBERT SACHS**

A N, a white man aged 64, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He fell and scraped his right hand on a wooden floor ten years ago. A number of splinters were removed, and later incisions were made over several fluctuant areas, with evacuation of pus. Since then there have been periodic swellings, many of which have opened spontaneously. Dark granules, of various sizes and having resemblance to foreign bodies, were frequently noted in the pus. A microscopic examination shortly after the onset showed a foreign body reaction in the tissues. Three months before admission, after striking his hand, swelling of both the palm and the back of the hand occurred.

Examination reveals many sinus tracts in the palm, from which pus can be expressed. The pus contains many dark granules varying in size from that of the head of a pin to that of a split pea. The granules are irregular and for the most part angular. The back of the hand shows several subcutaneous swellings, which are firm, movable and not attached to the skin. No sinus tracts lead from these swellings.

Microscopic examination of the granules showed a rather coarse mycelium. A cultural growth was obtained with difficulty, the fungus was probably a species of *hormodendron*. Histologic studies showed the black granules in the tissues from specimens of the palmar lesions and of a deep subcutaneous nodule on the back of the hand. Roentgen studies showed the bones to be unaffected in the disease process. The Wassermann reaction of the blood was negative. A complete blood count and a urinalysis revealed no abnormalities.

DISCUSSION

DR GEORGE M MACKEE I agree with the diagnosis of deep fungous infection because of the microscopic demonstration of mycelium, and I accept the diagnosis of mycetoma, because it was made by a good mycologist.

DR WILBERT SACHS When I saw this patient, the first thing that was apparent was the clublike appearance of the extremity. I saw the patient reported

on by Drs Gammel, Miskdjian and Thatcher (*ARCH DERMAT & SYPH* **13**: 66 [Jan] 1926) and though the lesion was on the foot the same feature was striking. In this patient, besides the clublike appearance of the hand, there were many vesicular lesions, some containing black granules and others yellow. With these features, the diagnosis of mycetoma was suggested. If the lesions were on the foot instead of the hand, I believe the diagnosis would be much more evident. Cases of mycetoma of the hand have been reported in the literature (Pels, I. R. *J. Cutan. Dis.* **37**: 740, 1919).

DR E. WILLIAM ABRAMOWITZ: I have observed only 1 such case before, and in that the lesion was on the foot of a Negro. I am interested to know what treatment, if any, is effective.

DR WILBERT SACHS: Regarding treatment, the books recommend iodides and at times amputation. Dr. Cole's patient was hospitalized for a long time, and even with all types of therapy, improvement was not noticeable.

DR ANTHONY C. CIPOLLARO: I should think this would be a favorable opportunity to give ethyl iodide inhalations. If the inhalations are carefully given, I do not believe that this form of therapy would be dangerous, even if used for elderly patients.

DR GEORGE M. LEWIS: The granules are protected by a hard capsule, and this has to be pierced before medication can be effective. At present we are administering iodides intensively. Amputation is sometimes necessary if there is involvement of bones. We have not yet definitely classified the micro-organism.

Dermatitis Herpetiformis Treated Successfully with Sulfapyridine. Presented by DR MAURICE J. COSTELLO

A. C., an unmarried woman aged 22, was presented before this society on May 9, 1939 (*ARCH DERMAT & SYPH* **41**: 134 [Jan] 1940). In April 1939 she was given $7\frac{1}{2}$ grains (0.48 Gm.) of sulfapyridine three times a day for one week and then twice a day for the following week. The eruption, which was unusually severe, completely disappeared in about three weeks. There has been no recurrence. The areas of localized residual pigmentation and superficial scarring persist.

DISCUSSION

DR E. WILLIAM ABRAMOWITZ: I presented before the class at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital a patient with dermatitis herpetiformis who showed great improvement after taking sulfanilamide. I tried giving it in 2 other cases, with similar results. It is not necessary to order the large doses that are being used for severe systemic conditions. I have not used sulfapyridine. It is hoped that no recurrences will develop when administration of the drug is discontinued.

DR GEORGE M. MACKEE: In my experience, sulfanilamide and sulfapyridine in dermatology have been uncertain drugs. One sees occasional good temporary results in pemphigus, erythema multiforme, lupus erythematosus, acne varioliformis, sycosis, vulgaris, dermatitis herpetiformis and even acne vulgaris, but failure is common. They are used because sometimes the results are satisfactory. Some people can take these drugs with no unfavorable reaction, while others cannot.

DR HOWARD FOX: I saw this patient with Dr. Costello when she presented a typical picture of Duhring's disease of five years' duration. Shortly after treatment with sulfapyridine new lesions ceased to appear, and the condition has not recurred for the past eight months. The result was striking, and I think sulfapyridine merits a trial in other cases of this rebellious disease.

DR MAURICE J. COSTELLO: I agree with Dr. Fox that there was relief of itching and remarkable improvement in this patient's eruption within three days after the initial dose of sulfapyridine. In two weeks there was complete disappearance of all the active lesions, and itching was absent. It is interesting to note that the patient has remained free of the eruption in spite of the fact that

administration of the drug has been discontinued now for seven months. The residual hyperpigmentation in localized areas bears evidence of the severity of the eruption, which had been present for five years.

Lichen Planus, Severely Excoriated Presented by DR MAURICE J COSTELLO

A S, a woman aged 62, was born in Germany. She is of nervous temperament. She had an appendectomy five years ago and excision of a lipoma four years ago. The duration of the present eruption is two years. It has become worse in the past month. It appeared first on the flexor aspects of the wrists and the inner aspects of the thighs.

The eruption she now presents is generalized except that there are no lesions on the face and neck. The interesting feature of this eruption is severely excoriated lesions resembling those of pediculosis corporis. In several areas can be seen the typical, shiny, umbilicated, flat papules of this disease. The oral lesions are characteristic. The Kobner phenomenon is present.

DISCUSSION

DR HOWARD FOX: Lichen planus resembles pityriasis rosea in one respect. In some cases there is moderate itching, in others the itching is severe, and in some there is no itching at all—at least, in the average case of lichen planus one does not see many scratch marks. The case presented today happens to be one in which the skin has been severely excoriated.

Melanocarcinoma Presented by DR MAURICE J COSTELLO

A T, a man aged 23, was presented before this society a year ago (*ARCH DERMAT & SYPH* 40 298 [Aug] 1939). He is presented this evening to show that his course since then has been favorable. His weight has been normal, and he is without symptoms. Examination does not disclose any new lesions or metastases to the neighboring lymph glands.

Treatment has consisted of irradiation with radium of the lower half of the left ear and the preauricular and postauricular regions, as well as the regional cervical and axillary lymphatic glands. In addition to the malignant melanoma lesion, which is smaller than it was last year, he has a mild radium dermatitis.

Melanocarcinoma Following the Treatment of a Common Mole Presented by DR MAURICE J COSTELLO

A S, a white girl aged 18, presented herself on April 14, 1936, when she was 14 years old, for treatment of a pigmented, dark brown, hairy common mole, measuring $1\frac{3}{4}$ by $1\frac{1}{2}$ inches (4.45 by 3.8 cm) and located on the left side of the nose. There had been no increase in size or in pigmentation prior to this time. She wished to have it removed because it was a cosmetic deformity. Its size and location made complete surgical excision inadvisable. The lesion was treated by electrodesiccation on April 21, May 5, June 16 and July 7, 1936. On July 14, July 28 and September 15 it was treated by the application of solid carbon dioxide for ten to fifteen seconds, with moderate pressure. The patient was observed on March 25, 1937. The cosmetic result was good. The treated area was light red.

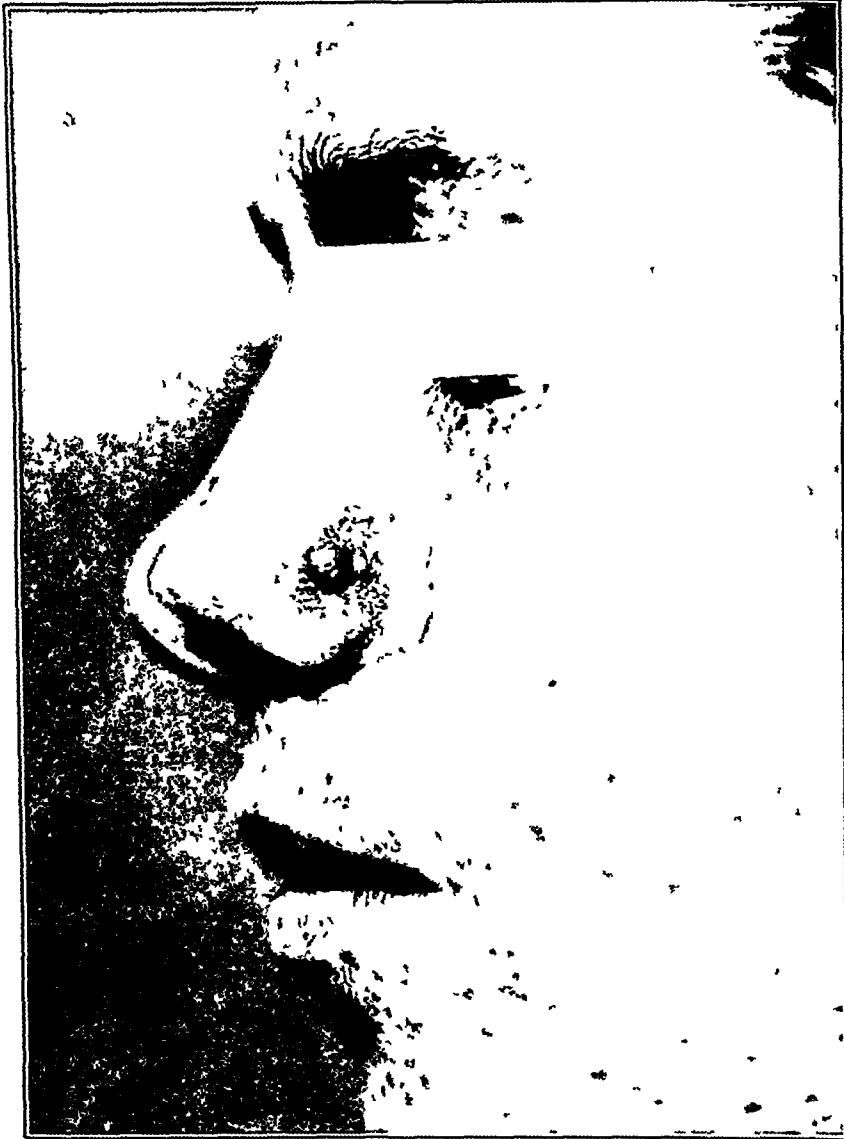
On April 27 in the center of the aforementioned site was a rounded pea-sized, blue-black lesion, which the patient claimed appeared two weeks previously. A clinical diagnosis of malignant melanoma was made, and because of delay in the biopsy report the lesion was irradiated with radium. It received 500 milligram hours, and the regional cervical lymphatic glands, 12,000 milligram hours.

She was examined on July 12, 1937. The wound inflicted during removal of tissue for biopsy had healed, and melanotic pigment was scattered through the surrounding skin. The report of the histologic examination by a general pathologist showed "an irregular hyperplastic, well differentiated, stratified squamous epithelium, with long coarse papillae and an underlying derma of dense hyaline fibrous tissue, which supports a moderate number of large uniform nevus cells."

and a great number of deeply pigmented chromatophores" The diagnosis was "pigmentary nevus"

Roentgenograms of the lungs, bony thorax and osseous part of the nose were normal

The patient was not seen again until November 1939 In the interim, she enjoyed good health, and the lesion on her nose had changed little There were



The area enclosed by the ink line is the former site of a common mole The melanocarcinoma in the center appeared one year after treatment

increased punctate and pinhead-sized bluish black satellites surrounding the pea-sized solid lesion A careful examination revealed no new pigmented lesions on her body, although, as the photograph shows, she had numerous dark brown freckles which had been present since early childhood

The appearance of the lesion, which had not changed, suggested a reexamination of the histologic specimen Dr Symmers, Dr Johanssen and two dermatopathologists, Dr Satenstein and Dr Sachs, concurred in the histologic diagnosis of melanocarcinoma

DISCUSSION

DR GEORGE M MacKEE This patient interests me because of the fact that the original diagnosis was common hairy pigmented mole I do not believe that

the original diagnosis was correct. All physicians have different conceptions about just what is meant by the term "common mole," which, incidentally, is a poor designation. I personally have never seen malignancy following what I call a common mole. I think the lesion was a benign melanoma which became a malignant melanoma. It is not rare to have roentgen rays or radium in large doses delay the process or make it quiescent or, on occasions, effect a cure. However, this lesion is not cured. It is still present, and I should think, for the protection of this patient's future, that it would be well to institute surgical treatment.

DR ANTHONY C CIPOLLARO I should like to confirm what Dr MacKee said. Statements are frequently made that malignant melanomas arise from ordinary common moles. This is contrary to the experience of many of the older dermatologists who have had many opportunities to observe many patients after treatment with various methods.

DR E WILLIAM ABRAMOWITZ When a patient presents himself with a brown, elevated, pigmented mole with no hair growing in it, I never feel certain that it is *absolutely safe for me to go ahead and remove it, except surgically*. But when it is on the face of a woman, I always feel that the responsibility should be shared by having another opinion before any procedure is undertaken. The French dermatologists say that this type of lesion can be treated safely with electrolysis.

DR DAVID BLOOM I have observed the patient from the start, and I recall the nevus as an infiltrated plaque on the lower part of the left side of the nose, dark brown and having fuzzy hair. It was not the usual circumscribed, pigmented, hairy nevus which is seen frequently and which one does not hesitate to treat. This case has impressed me so that in the future I shall look on such plaques as potentially malignant or at least give a guarded prognosis.

DR PAUL E BECHET The question as to the advisability of removing pigmented moles comes up with definite regularity at many dermatologic meetings and probably will continue to do so in the distant future. Personally, I am guided by the color and number of moles present. In the presence of dark, elevated, bluish black nevi, either single or multiple, or when there are dozens of nonhairy moles on the face and even on the body, I prefer not to intervene. On the other hand, I have, over the space of many years, removed hundreds of pigmented moles, both hairy or nonhairy, without noting a single instance of subsequent malignancy. I believe that the development of malignant tissue after the removal of a pigmented mole can be greatly obviated by thoroughness in its removal. Most of the disastrous results that I have noted apparently followed inadequate removal and inappropriate technic. Squeezing, scratching and picking moles are not uncommon habits even among intelligent women and are also important causative factors in malignant change. I have so frequently listened to a discussion of the subsequent dangers of intervention and so seldom observed them that I am greatly inclined to believe that physicians suffer too much from the fear of malignancy. Dr Costello's case, however, proves that in rare instances this fear is not entirely unwarranted.

DR WILBERT SACHS It is quite possible that the original diagnosis as well as the one presented tonight are both correct. It is not uncommon to find a combination of nevi in a single specimen. This patient may have a junction type nevus in combination with one of the other types of epithelial nevi.

After looking at the slide, it is gratifying to see that this patient is not only alive but apparently in good health. The microscopic picture is that of a nevocarcinoma.

DR HOWARD FOX I recall when the girl was first presented at our weekly conference at Bellevue Hospital as having an ordinary pigmented and hairy nevus of the side of the nose. At that time the hair covering the nevus was definitely profuse and long. Orders were given to treat her with solid carbon dioxide or by electrodesiccation. When I saw her later, I was shocked to see a lesion that was clinically a nevocarcinoma. This was the first time I had seen a malignant

growth develop after proper treatment of an ordinary pigmented and hairy nevus I consider this a unique case

DR DAVID L. SATENSTEIN I have not seen any, read any or heard of any reports of a cutis type nevus eventuating in a malignant growth Here is a case of a nevus that supposedly turned out to be a junction type It was a junction type from the start, taking the clinical picture of a common mole in the beginning These mistakes have been made often, but our attention has not been called to them

DR MAURICE J. COSTELLO This patient had been seen by the members of the Dermatologic Staff at Bellevue Hospital before the original lesion was treated, and the consensus of those present was that the patient had a pigmented, dark brown, hairy mole The same group agreed that the blue-black, pea-sized, elevated nodule which appeared one year after treatment of this mole was clinically a malignant melanoma, and the diagnosis was confirmed by histologic study

Parapsoriasis Varioliformis. Presented by DR MAURICE J. COSTELLO

H. C., a married laborer aged 26, has had an eruption almost continuously for twenty years No member of his family is similarly affected

The patient presents a chronic, generalized, extensive eruption, consisting of flat and scaly papular lesions resembling both pityriasis rosea and lichen planus He also has a number of vesicles and papulovesicles There are vesicular lesions in the mouth on the buccal mucosae, the hard and soft palates, the tongue and the lips The glans penis is occasionally similarly affected Scaly, flat papular lesions are seen on the scalp, palms and soles There are a number of punched-out and irregular lentil-sized cicatrices on his face

A histologic examination confirmed the diagnosis of parapsoriasis varioliformis His Wassermann reaction was negative He had gonorrhea in 1934

His treatment has consisted of intravenous injections of typhoid vaccine in graduated doses, solution of potassium arsenite U. S. P. and various salves and lotions, as well as ultraviolet irradiation

DISCUSSION

DR E. WILLIAM ABRAMOWITZ I think that this case is one of parapsoriasis, but I am not certain that the condition is the varioliform type

DR PAUL GROSS The condition is chronic parapsoriasis with occasionally pure varioliform lesions It is this type of eruption that forms a link between the chronic and the acute varioliform parapsoriasis Another lesion found in both varieties is the small lichenoid flesh-colored papule, which was described by Wallhauser many years ago

DR MAURICE J. COSTELLO I have observed this patient for about seven months The lesions of this polymorphous eruption resemble pityriasis rosea and lichen planus, while other lesions are vesicular During the periods of exacerbation the vesicular element predominates The patient claims that up to the present time ultraviolet irradiation has given him the greatest relief

GEORGE C. ANDREWS, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Jan 9, 1940

Lichen Planus Followed by Lichen Pilaris (Vitamin A Deficiency?). Presented by DR E. WILLIAM ABRAMOWITZ

Mrs. T. B., aged 32, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital Typical lesions of lichen planus

developed about four months ago. The eruption was generalized, and she had considerable itching. The patient received injections of sodium arsenate and roentgen ray therapy, the latter being applied not only to the affected areas but to the spine.

After one month of treatment, grouped lichen pilaris lesions began to appear on different parts of her body, and also some pigmented elevated tags became noticeable on her neck and trunk. The administration of sodium arsenate was then discontinued. She never had any lesions in her mouth.

The patient has been eating only one meal a day.

The diagnosis is lichen planus followed by lichen pilaris or cutaneous lesions due to vitamin A deficiency.

DISCUSSION

DR HOWARD FOX I think it is possible that this eruption is due to vitamin A deficiency and suggest that the patient be tested for night blindness.

DR MAX SCHILLER I think that the keratosis pilaris is due to avitaminosis. I questioned her as to the contents of her one meal a day. She stated that she ate little or no butter, and there was almost a complete absence of vitamin A in her diet. Furthermore, the distribution of the lesions, for example on the forearms and trunk, are in favor of vitamin A deficiency in this case.

DR ISADORE ROSEN I should not associate this generalized lichen-pilaris-like eruption with a vitamin deficiency. In view of the fact that this patient has had therapy which included arsenic sufficient to influence the extensive lichen planus, I should be inclined to associate the present eruption with the arsenic that she has received.

DR MAX SCHEER The patient stated that her diet included oils, fats, vegetables and meat. The oils, like olive oil and salad oil, contain at the most only faint traces of vitamin A. There is none in meat and practically none in the vegetables that she eats. The only sources from which she could get it are eggs, butter and milk, mainly butter, and she does not eat any butter.

DR MAURICE J COSTELLO Patients are occasionally seen at Bellevue Hospital with keratotic papular lesions similar to those in this case, and I have never obtained a history of inadequate vitamin intake. This afternoon I saw 2 brothers, 7 and 9 years of age, 1 of whom had an eruption which clinically resembled those which have been described as due to vitamin A deficiency, the other child's skin was normal. A history of vitamin deficiency in these cases is rare. Regarding associated night blindness, none of those seen by me have had clinical manifestations of this condition. They were not tested by means of the photometer. I think that many of the conditions referred to as vitamin A deficiency are not that at all. Are all patients able to utilize their adequate vitamin intake?

DR LUDWIG OULMANN While I do not believe that this case is one of vitamin A deficiency, I think it would be easy to prove this by administering vitamin A.

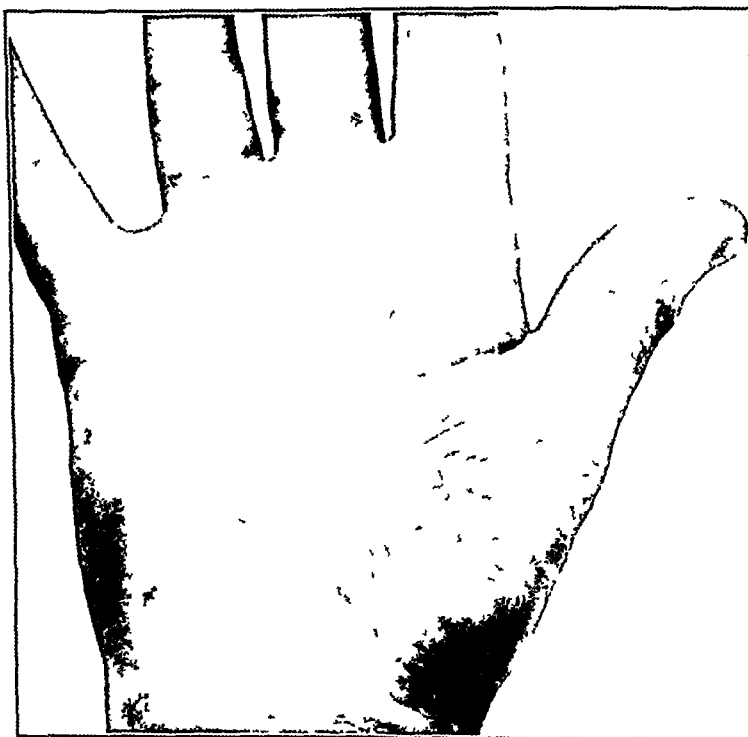
DR PAUL E BECHET In my opinion the keratosis pilaris in this patient bears no relation to the old lichen planus. They are two entirely different conditions.

DR ANTHONY C CIPOLLARO Knowledge of the relation of vitamin A deficiency to cutaneous eruptions is of recent origin. The cases described by Frazier and Hu (Frazier, C N, and Hu, C-K. *Nature and Distribution According to Age of Cutaneous Manifestations of Vitamin A Deficiency. A Study of Two Hundred and Seven Cases*, *ARCH DERMAT & SYPH* 33 825 [May] 1936) are examples of decided vitamin A deficiency and general malnutrition. I think it is a mistake to jump to the conclusion that all patients presenting keratotic lesions on the extensor surfaces have vitamin A deficiency. Before the establishment of a definite diagnosis, patients should present not only keratosis but also evidences of a deficiency of vitamin A in the blood and night blindness. The history, moreover, must reveal that the diet has been lacking in vitamin A.

DR DAVID L SATENSTEIN There are many persons who do not take plenty of vitamins but who do not have any disturbances Many persons stay out in the sun and do not get lupus erythematosus, and in some lupus erythematosus develops after a sunburn

A Case for Diagnosis (Lichen Moniliformis?). Presented by DR WILBERT SACHS

Miss H D, aged 22, was first seen by me at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec 2, 1939 She stated that two years ago the eruption developed on her palms At first there were only a few lesions present, but the number has been slowly but steadily increasing She has never had any subjective symptoms



A case for diagnosis (lichen moniliformis?)

The patient now presents an eruption on the palms, especially on the thenar surface and somewhat on the hypothenar surface There are numerous discrete pearly white papules from 1 to 3 mm in diameter They are firm and in some areas are arranged in rows In the past two months similar lesions have developed along the folds of the fingers

Histologic examination showed a neurodermatitic type of reaction No definite diagnosis could be made

DISCUSSION

DR HOWARD FOX I doubt whether this condition is a naevus tardus, on account of the bilateral distribution It is also not a neurodermatitis, because of the entire lack of subjective symptoms and the absence of signs of inflammation I do not know how to classify the eruption

DR DAVID BLOOM Considering that the biopsy was performed on material from the thenar area and not from the palm itself, the hyperkeratosis seen under the microscope is pathologic and is the only conspicuous feature The lesion should therefore be classified as some unusual form of papular keratosis

DR ISADORE ROSEN While I have not seen the histologic specimen of this case, I should make a diagnosis of *verruca plana*. There is also one lesion on the hand which clinically suggests *verruca vulgaris*.

DR LUDWIG OULMANN In my opinion lesions which look similar to but are not *verrucae planae* are seen more frequently, especially on the thenar and hypothenar areas of the palms. They spread and are itchy. I believe this condition is a contact dermatitis with keratinization.

DR MAURICE J COSTELLO I agree with Dr Rosen's conception of this case. This patient has an ordinary *verruca* on the hypothenar eminence of the right palm, in addition to the eruption described by Dr Sachs. I am not sure that the lesions on the thenar eminence are *verrucae planae*. I think that all the lesions are *verrucae* and that the difference in appearance is due to the difference of location on the palms, the skin of the hypothenar eminence being thicker than that of the thenar.

DR DAVID BLOOM The clinical and, as I understand, the histologic observations exclude the diagnosis of *verruca*.

DR WILBERT SACHS Clinically these lesions do not impress me as being hyperkeratotic. They are smooth, and although they appear vesicular they are really solid. The biopsy specimen was taken from the palm, where the horny layer is thick. While there is some increase in the thickness of the horny layer, it is not enough to indicate a keratoma of any type. I also thought of the possibility of lichen albus, but there is no microscopic evidence to corroborate such a diagnosis. There is no suggestion of *verruca* in the histologic slide.

Monilial Paronychia Presented by DR PAUL E BECHET

E. A., a woman aged 38, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec 26, 1939, with an eruption on the tips of her fingers of four years' duration.

On examination the finger nails show discoloration, loss of luster, transverse striations and ridges and crumbling lateral edges. The tissue proximal to the nails is swollen, reddened, indurated and painful. Occasionally pus exudes from the nail beds.

Monilia albicans were cultured from the finger nails. Smears and cultures from all other parts were negative, including those from the tongue and stool.

Wassermann and Kahn reactions were negative.

DISCUSSION

DR DAVID BLOOM My conception of these cases has always been that the condition is due to persistent exposure to water and insufficient drying of the hands, with the formation of a favorable soil for the growth of *Monilia*.

DR HOWARD FOX The patient has ordinary paronychia, with resulting dystrophic changes in the nails. It is well known that this disease may be due to pyogenic cocci or to *Monilia*. I should like to know whether the presence of the causative organism is indicated by the appearance of the dystrophic changes.

DR ANTHONY C CIPOLLARO Soap and water are said to accentuate this condition. In my opinion, this is based on uncertain grounds.

I think that this case is suitable for treatment with ethyl iodide inhalation.

DR MAURICE J COSTELLO I see this condition frequently in women who prepare salads and in waitresses whose occupation necessitates the frequent immersion of the hands in water. I believe that soap and water make it worse.

DR MAX SCHEER I have seen such eruptions in men whose occupation was such as that of bartender or dishwasher, and they have been all ages and all races.

DR GEORGE C ANDREWS I also believe that it is deleterious to keep the skin saturated with water.

DR PAUL E BECHET I have observed a sufficient number of cases with the same symptoms and believe that monilial infection of the finger nails presents a definite clinical picture, which is not infrequently corroborated by the demonstration of *Monilia albicans*. The paronychia is characterized by induration, swelling and redness just proximal to the nails. Pus is uncommon, and there is little pain. The nails are striated and ridged, and their lateral edges crumble easily and are brownish. Erosion in the webs of the fingers may or may not be present. Monilial paronychia and onychia occur most frequently in stout women who do much laundry work and dishwashing. It is much rarer in men, and when it does occur it is much more common in bus boys, waiters and dishwashers.

Pigmentation of the Mouth from Bismuth Presented by DR MAURICE J COSTELLO

G W, a housewife aged 19, born in New York, presented from Bellevue Hospital, had a chancre of the lower lip in October 1939, in which spirochetes were demonstrated by dark field examination. This was followed by a secondary lenticular papular syphilid. The Wassermann reaction of the blood at that time was 4 plus. In the latter part of November she was delivered of an apparently normal infant. Since that time she has received five injections of neoarsphenamine, five injections of bismuth subsalicylate and seven injections of bismarsen. Since her admission to the hospital she has had two injections of mapharsen. Discrete pinpoint-sized to pinhead-sized areas of black pigmentation form pea-sized patches on the tip of the tongue where it comes in contact with the bismuth line of the lower gums. Similar areas are also present on the inner surface of the lower lip. There are a few discrete pigmented lentil-sized areas of pigmentation on the hard palate.

DISCUSSION

DR DAVID BLOOM Pigmentation of the tongue due to bismuth must be rare, for this is the second case I have ever observed. A similar case with pinpoint-sized pigmented spots on the anterior aspect of the tongue I observed a few weeks ago at the New York City Hospital.

DR HOWARD FOX I saw pigmentation of the mouth but no evidence of stomatitis. While pigmentation following bismuth therapy is extremely common along the margin of the gums, it is decidedly rare on the tongue.

DR MAX SCHEER I agree with those who think this condition is pigmentation and not stomatitis, and for that reason I do not think it is necessary to stop the administration of bismuth. However, the dose should be reduced to one half, in that way, the pigmentation will subside and gradually disappear.

DR MIHRAN B PAROUNAGIAN I never saw such decided pigmentation on the tongue as this patient presents. I have seen the condition in a number of patients on the gum line but not as pronounced as this. If I were treating the patient, I should discontinue administration of bismuth and give mercury.

DR S GELLIS (by invitation) I have heard it said that pigmentation indicates that a good bismuth preparation is being used, and many suggest that the administration should be continued as long as the drug produces no general harm to the patient.

A Case for Diagnosis (Pyoderma? Iododerma?) Presented by DR MAX SCHEER

B A C, a white school girl aged 17, born in the United States, was seen at Mount Sinai Hospital, service of Dr I Rosen, for an eruption on the legs of four and one-half months' duration.

The eruption began as small superficial papulopustules, which gradually enlarged until they attained a diameter of 2 to 3 inches (5 to 7.5 cm). The lesions were predominantly on the posterior aspects of the calves and ankles. They varied

from $\frac{1}{2}$ to 3 inches (13 to 75 cm) in diameter and were superficial, slightly indurated, sharply defined, circinate, bluish red and plaque-like, not raised. One of the larger lesions had three pinhead-sized openings, which oozed creamy pus. The lower margin of the largest lesion was eroded. As old lesions healed, new ones appeared, so that there are small papulopustules, various-sized circinate plaques and slightly atrophic and pigmented areas.

The patient had been taking iodized salts but no medication.

The blood count showed normal results. The sedimentation rate was 18 mm in one hour. The Wassermann reaction of the blood was negative. Graded tuberculin tests showed normal sensitivity. The report of the histologic examination was "Skin showed necrosis and nonspecific inflammation within the corium and ulceration." The report of a later examination was "A definite diagnosis of Bazin's disease cannot be made, but an erythema-nodosum-like lesion is conceivable. A fungous infection or a drug eruption should be ruled out. No tubercle bacilli were seen."

In spite of the cessation of ingestion of iodized salts, new lesions are constantly appearing.

DISCUSSION

DR ANTHONY C CIPOLLARO. The clinical features are those of iododerma. I cannot see any evidence of Bazin's disease.

DR HOWARD FOX. It is often necessary to differentiate bromoderma or iododerma from some type of tuberculosis, such as papulonecrotic tuberculid. I think a useful point of differentiation is tenderness, which is present in bromoderma and iododerma.

DR MAURICE J COSTELLO. I agree that this condition is probably a drug eruption, and I suggest that the urine and blood be examined for iodides and bromides.

DR MAX SCHEER. I mentioned Bazin's disease, first, because that was the diagnosis suggested by my associates in the clinic and, secondly, to arouse some discussion. Personally I do not think the condition is Bazin's disease, because I could follow the lesions from their incipency up to their full development, and none developed subcutaneously and then approached the surface. They began as superficial pustules, which spread to form large plaques. My diagnosis is a drug rash, probably an iodide eruption.

Amelanotic Melanoma Presented by DR MAURICE J COSTELLO

R S, an Austrian Jewess, a housewife aged 50, presented from Bellevue Hospital, was previously presented before the New York Academy of Medicine, Section of Dermatology and Syphilis, on Jan 2, 1940 (*ARCH DERMAT & SYPH*, p 175).

DISCUSSION

DR DAVID BLOOM. When the patient was previously presented the dark, pigmented lesion in the center made me consider first of all the diagnosis of malignant melanoma with dissemination, in spite of the nonpigmented satellite lesions. I did not consider lymphangioma circumscriptum, because, among other points, the age of the patient at which the lesion appeared did not conform with that diagnosis.

DR S GELLIS (by invitation). When this patient was admitted to my ward at Bellevue Hospital, I entertained the diagnosis of either Kaposi's sarcoma or hemolympangioma circumscriptum. One of the lesions was punctured, and it was found to be solid. The patient left the hospital for a short time, and when she returned new lesions were noticed on the front of her leg. Dr Fox and Dr Bloom suggested the diagnosis of melanoma. I should like to have suggestions as to treatment.

DR J FRANK FRASER. I prefer the term amelanotic melanoma.

DR WILBERT SACHS At the meeting of the New York Academy of Medicine, Section of Dermatology and Syphilis, I thought the condition was Kaposi's sarcoma. I should not make that diagnosis tonight, after hearing the pathologic report. Since in the microscopic description there is no mention of any changes in the lower border of the epidermis, I suggest that Perl's test be done to see if the pigment is melanin or iron.

DR DAVID L. SATENSTEIN Might I refer to Broder's classification of neoplasms? The patient has a better chance to live if the lesions are not excised. If radical surgical intervention is done, it must be amputation. Radium might do some good. I am not so sure that this patient will die, because I have seen patients with these lesions that are still alive after long periods. Not all cases of melanoma are fatal.

DR MAURICE J. COSTELLO The biopsy specimen was taken from the original lesion, which at that time was moderately pigmented. I think that the title under which this case is reported should indicate the fact that some of the lesions are melanotic and some clinically are nonpigmented. In the beginning the clinical diagnosis was difficult, because most of the lesions were nonpigmented and they suggested lymphangioma circumscriptum or Kaposi's sarcoma. The patient has had no treatment.

Charcot's Disease of the Ankle. Presented by DR MAURICE J. COSTELLO

G. F., an unemployed man aged 41, born in the United States, presented from the wards of Bellevue Hospital, gives no family history of syphilis. A painless swelling of the right ankle appeared four months ago. When he was admitted to the hospital, in addition to the aforementioned symptoms, examination of the joint showed crepitus and hypermobility, which were not accompanied by tenderness. Roentgenograms of the right ankle showed a fracture along the dorsal aspect of the right tarsal scaphoid, with backward displacement of the fragments. There is an extensive periarticular infiltration of the soft parts.

The patient has recently received malarial therapy for syphilis of the central nervous system. The Wassermann reaction of the spinal fluid was 4 plus, and the colloidal gold curve was tabetic in type. For the past ten months he has had lightning pains in his lower extremities and urgency of urination. In addition to malarial treatment, he has been given bismuth subsalicylate intramuscularly and sodium iodide intravenously. Therapy has had no beneficial effect on the ankle.

DISCUSSION

DR S. GELLIS (by invitation) When this patient was first admitted to the hospital he complained of pain about his ankle, especially on pressure, over the medial aspect of the right scaphoid. He gave no history of injury to his foot. After a few days in the ward the pain disappeared, and manipulation of his ankle caused no pain, although definite crepitus was elicited. Further roentgenograms showed Charcot joint with fragmentation of the previously reported fracture. The orthopedic surgeons recommended an ankle fusion.

DR MAURICE J. COSTELLO I think this patient has a Charcot joint, because of the lack of pain, the preternatural mobility and the clinical and roentgenologic appearance. I do not think that the destruction has caused complete involvement of the tarsal bones.

Aberrant Hair on the Mucous Membrane of the Lower Lip Presented by DR MAURICE J. COSTELLO

W. K., an electrician aged 46, born in New York, presented from Bellevue Hospital, gives no family or personal history of congenital abnormalities. About three months ago the patient felt with the tip of his tongue a hair on the mucous

membrane of the lower lip. He thought it was a tooth brush bristle, which it resembled. He pulled it out and found two hairs with their sheaths. Three weeks later he removed a hair of similar appearance from the same location. This phenomenon was repeated three times in three months. The hair in this location was $\frac{1}{2}$ inch (1.3 cm) in length, coarse and colorless. Microscopically it proved to be a terminal unpigmented hair.

DISCUSSION

DR DAVID BLOOM. It would be of interest to study this hair under the microscope to see if it differs in any respect from the hair on the skin.

DR LUDWIG OULMANN. Fifty years ago Max Joseph (*Lehrbuch der Haut- und Geschlechtskrankheiten*, ed 2, Leipzig, Georg Thieme, 1895) mentioned the presence of hair in combination with sebaceous glands in the mucous membrane of the lip, Audry (*Monatschrift für prakt Dermat* 29 101, 1899) and Bergière mentioned the presence of hair in the mucous membrane.

Recklinghausen's Disease Associated with Eighth Nerve Deafness Presented by DR MAURICE J COSTELLO

J. B., an unemployed Irish-American man aged 38, states that there is no family history of Recklinghausen's disease. I have not examined other members of the family. The duration of the eruption is twenty-five years. It is generalized and consists of soft pedunculated herniated fibromas and irregular areas of café-au-lait pigmentation, characteristic of this disease. He also has similar lesions on the tongue and soft palate. He has had total deafness of the left ear for the past four years, which an otologist stated is due to a fibroma involving the eighth nerve. He has asymptomatic neurosyphilis. He had a chancre eighteen years ago. The Wassermann reactions of the blood and spinal fluid were positive, and the colloidal gold curve was 0001221000. Antisyphilitic treatment at present consists of injections of mapharsen.

DISCUSSION

DR DAVID BLOOM. While the commonest lesions of Recklinghausen's disease are pigmentation, tumors of the skin, peripheral nerves and cranial nerves are occasionally encountered and are often discovered at autopsy. Bilateral tumors of the acoustic nerve causing sometimes complete deafness have been reported. In order to state definitely that no other member of the family is affected, one has to examine personally all the members, for pigmentation and a few cutaneous tumors are usually overlooked or ignored.

DR ISADORE ROSEN. This case is interesting because all types of complications are frequently seen associated with Recklinghausen's disease. I recall an instance in which the late Dr. Goldenberg was called in to see a patient in the urologic service of Mount Sinai Hospital for some renal condition. The patient had the clinical symptoms of mild Recklinghausen's disease, in the discussion of the case Dr. Goldenberg emphasized the importance of looking for malformations of the kidney, as they occasionally occur in connection with that disease. It was found that the patient had a horseshoe kidney, and it was fortunate that the condition was recognized before surgical intervention was done.

DR J. FRANK FRASER. I agree with the otologist whose theory is that the deafness in this case is due to neurofibroma involving the eighth nerve. The peripheral nerves of the skin are not the only ones involved in the course of Recklinghausen's disease, and physicians are all aware of the deformities due to involvement of the spinal nerves. Involvement of the cranial nerves also occurs and much more frequently than is generally supposed.

In regard to prognosis, one must keep in mind the fact that sarcoma develops in about 13 per cent of all cases of Recklinghausen's disease. The percentage in Geschichten's series was 20 per cent. I have observed 2 cases of subepidermal sarcoma in Recklinghausen's disease during the past year.

DR MAURICE J COSTELLO I have seen several patients who had foot drop resulting from osseous rarefaction of the vertebral column in the lumbosacral region

Scleroderma, Sclerodactylia Presented by DR E WILLIAM ABRAMOWITZ

O H, a married man aged 25, was first presented before the New York Academy of Medicine, Section of Dermatology and Syphilis, on March 4, 1924 (ARCH DERMAT & SYPH 10:368 [Sept] 1924) Subsequently I presented him at another meeting in 1926 (ibid 15:353 [March] 1927) The last presentation was by Dr Bloom in 1930 (ibid 22:928 [Nov] 1930)

At present all the fingers and toes are shriveled The skin in these areas is hidebound and livid The extensor area of the right elbow also shows a scleroderma, with apparent calcification The rims of the ears and the tip of the nose are partially destroyed and atrophic The patient has always had a tendency to have cutaneous infections Recently cutaneous abscesses have developed on the spine and over other bony prominences, and because of his poor nutrition these abscesses break down and form ulcers which are slow in healing He is at present receiving vitamins A and D in addition to a high caloric diet and local applications of gentian violet

The diagnosis is scleroderma confined to the terminal parts of the body, the underlying cause of which has not yet been determined, owing to the poor cooperation of the patient Various laboratory tests are now being performed

DISCUSSION

DR DAVID BLOOM This man was also presented in 1926 (ARCH DERMAT & SYPH 15 353 [March] 1927) before the Brooklyn Dermatological Society He was first presented (ibid 10 368 [Sept] 1924) as having acrodermatitis pustulosa hiemalis, because of ulcers and exacerbations during cold weather A diagnosis of epidermolysis bullosa was also considered, because the ulcers resembled broken bullae These diagnoses are not infrequently made in cases of sclerodactylia which are not recognized as such In 1930 I presented this patient (ibid 22:928 [Nov] 1930) with the diagnosis of progressive symmetric scleroderma One finds this term, particularly in the French literature, in contrast to generalized scleroderma, to designate those conditions which start with involvement of the fingers and toes, and may be confined to these and other distal areas of the body or may extend to the hands, wrists, forearms and other areas "Generalized scleroderma" spares, at least at first, the fingers and toes This patient shows, besides the acrosclerosis, also atrophy of the skin over the bony prominences of the elbows, vertebrae and shoulders, associated in some places with ulcerations

DR HOWARD FOX In my opinion, this case is by no means a typical one of scleroderma but a most unusual one In the ordinary case of scleroderma of the progressive type, the skin of the face is usually hidebound In this case it can be easily pinched up between the fingers

DR DAVID BLOOM The reason for the gangrene in this case, which led to loss of part of the fingers, nose and ears, is the hidebound condition of the skin, leading to atrophy and destruction of the underlying soft tissues and bone In Raynaud's syndrome the cause of gangrene is the frequent constriction of the blood vessels Although the syndrome of Raynaud's disease may be present in cases of scleroderma, for both conditions are due to disturbance of the vegetative nervous system, this case cannot be designated one of "Raynaud's disease"

DR MAX SCHIER There are two types of scleroderma, the type that involves the trunk and later on may affect the face, and the type to which this case belongs, true acrosclerosis, which begins on the extremities and ends on the face and never involves the trunk or other parts of the body

DR GEORGE C ANDREWS There is a disease described as acrosclerosis, and I think this case fits into that category

NEW YORK ACADEMY OF MEDICINE, SECTION OF
DERMATOLOGY AND SYPHILISE W ABRAMOWITZ, M D, *Chairman*LEWIS B ROBINSON, M D, *Secretary*

Jan 2, 1940

Kaposi's Sarcoma Presented by DR LOUIS TULIPAN

M C, a Negro aged 56, presented from Bellevue Hospital, about nine months ago first noticed swelling and an eruption on the right hand. It then appeared on the left hand and shortly thereafter on the feet. The hands and feet were edematous, with multiple bluish nodules, pigmented patches and ulcerations, especially over the toes and fingers. He had been treated for syphilis at one of the city clinics during the year.

The Wassermann reaction of the blood on admission to Bellevue Hospital was 4 plus. Physical examination revealed nothing unusual except that the blood pressure was 102 systolic and 50 diastolic. The icteric index was 18, and the differential white blood cell count was normal. The patient complained of precordial pain. Roentgenograms of the hands showed generalized bony atrophy and flexion deformities of the fingers. Histologic examination of sections of the skin showed numerous dilated capillaries, with decided proliferation of connective tissue and many round and spindle cells, in places appearing sarcomatous. There were foci of hemorrhages in the surrounding tissue and hypertrophy of the horny layer.

About three months after admission to the hospital, after an attack of precordial pain, he became stuporous and died. The cause of death was coronary thrombosis.

DISCUSSION

DR CHARLES WOLF I take for granted that the histologic examination has proved the diagnosis. The interesting feature is the short duration of an extensive eruption of Kaposi's sarcoma. Kaposi's sarcoma is generally considered a slow, insidiously progressive disease.

DR EUGENE T BERNSTEIN I think that the coexisting syphilis can be regarded as a contributory factor in the spreading of the eruption, and the spreading to such an extent may be due to lessening of the resistance of the patient. I doubt, therefore, that ten months' duration disproves the diagnosis of Kaposi's sarcoma.

DR ISADORE ROSEN I wonder whether this patient has taken any iodides. It is well known that iodides may produce cutaneous lesions of all types. The lesions of Kaposi's sarcoma are usually slow in development, while those in this patient developed rapidly. I therefore suggest the possibility of a connection between this eruption and the treatment he has had for his syphilitic infection, which included arsenicals.

DR LOUIS TULIPAN The patient has had no iodides but has received the regular antisyphilitic treatment with a bismuth compound and arsenic.

DR MAURICE J COSTELLO The only therapy this man has received has been bismuth subsalicylate. He has had solution of potassium arsenite U S P only since his admission to Bellevue Hospital, which was three weeks ago. There has been no appreciable change in the eruption since that time.

DR LOUIS TULIPAN The interesting feature about this case is that Kaposi's sarcoma is extremely rare in Negroes. I think there are only about 4 or 5 cases reported in the literature. Again, there is the fact that the condition started on the hands instead of on the feet. In regard to the rapid development of the eruption and the destructive lesions, I believe that poor peripheral circulation may tend to rapid destruction and breaking down of lesions. One often sees lymphedema

and verrucous lesions in cases of Kaposi's sarcoma. Where there is poor peripheral circulation, as here, plus lymph stasis and edema, there might, therefore, be rapid destruction. I think that is the only plausible explanation.

A Case for Diagnosis (Kaposi's Sarcoma?) Presented by DR FRANK C COMBES

R. S., a woman aged 50, is presented from Bellevue Hospital, complaining of an eruption involving the right leg, of five months' duration. Examination shows over the lower part of the right leg a patch of closely aggregated papules varying in size from that of a pinhead to that of a pea and in color from pink to dark purple. There are also discrete lesions on the front of the leg which have appeared during the past week.

The Wassermann reaction was negative.

NOTE—Subsequent to this presentation, histologic examination showed a malignant amelanotic melanoma.

DISCUSSION

DR CHARLES WOLF: I should like to suggest the diagnosis of hemangiolymphangioma circumscriptum. The lesions appear hemorrhagic. They are soft, circumscribed and superficial. In the early manifestations of Kaposi's sarcoma the lesions are apt to be infiltrated. One does not see discrete vascular lesions, although there may be vascular lesions in accompaniment with the infiltrations. However, to find a discrete vascular lesion in a case of Kaposi's sarcoma is rare.

DR LEO SPIEGEL: I saw this woman about three or four weeks ago and my impression agrees with that of Dr. Wolf, that the condition is hemangiolymphangioma circumscriptum.

DR DAVID BLOOM: This woman impresses me as having a malignant melanoma, with less pigmented satellite lesions around a deeply pigmented primary lesion. The location and particularly the rapid development in a patient of such advanced age speak against the diagnosis of lymphangioma circumscriptum.

DR FRANK C. COMBES: I understand how the diagnosis of hemangiolymphangioma circumscriptum is entertained. That condition was the one I considered the first time I saw this patient, and I did not think of Kaposi's sarcoma as a diagnosis. The little nodules were pearly and looked like deep vesicles, but on being opened they were found to be solid. The age of the patient is somewhat against lymphangioma, it is usually seen in much younger persons. It is possible for lymphangioma to occur in this location, but it is more common on the upper parts of the extremities. I have never seen Kaposi's sarcoma, if the condition in this case proves to be that, at such an early stage, and I do not know just what it looks like at that time. One may see the angiomatous stage, in which there is little infiltration and little proliferation other than that which occurs in the blood vessels. The picture has changed some since this patient was first seen, and tonight the lesions are dusky red or blue, and there is scaling on some of them and some confluence. New lesions have appeared in the past few weeks, especially on the anterior part of the leg. In reference to melanoma, these lesions at their inception contain no pigment. They are clear and pearly. The pigmentation is secondary. In addition, there was no preexisting lesion of any type. The condition may be an amelanotic melanoma, but I do not recall having seen a patient with this condition.

Epidermolysis Bullosa Acquisita Presented by DR LOUIS TUIIPAN

S. B., a woman aged 57, presented from Bellevue Hospital, was previously presented at a meeting of the Bronx Dermatological Society (*ARCH. DERMAT. & SYPH.* 40:1016 [Dec.] 1939).

At present the patient exhibits few lesions, and in fact, this is the best she has been in the past year. There are remains of healed bullae on the dorsa of

the hands, the elbows, the buttocks and the right border of the tongue. On the extensor surfaces of the forearm are numerous grouped milia-like cysts. There are a few vesicles on the heels.

The patient was given large doses of viosterol in oil for three months, without effect. At present she is receiving 5 cc of concentrated liver extract weekly, she has been receiving this for the past fifteen weeks.

Epidermolysis Bullosa Presented by DR TIMOTHY J RIORDAN

A M S, a girl aged 2½ years, is presented from the New York Foundling Hospital. The eruption was first noticed when the child was 3 days old. It was located on the hands and feet, including the fingers and toes, and consisted of tense bullae arising from normal skin and erythematous areas covered by crusts resembling impetigo. Similar crusted lesions were scattered over the trunk and buttocks. There were many depigmented atrophic scars of previous lesions. No milia were observed.

DISCUSSION OF CASES OF DR TULIPAN AND DR RIORDAN

DR DAVID BLOOM The woman presented by Dr Tulipan has all the features characterizing epidermolysis bullosa dystrophica, namely, epidermal cysts, atrophy of the skin, involvement of the mucous membranes, with resulting scars, and dystrophy and shedding of the nails. The child presents the same condition, with greater intensity. In the first patient the term *acquisita* is not justified, and the term *tarda* should be substituted, for unless it can be proved definitely that the condition is due to some external agent, it should be considered hereditary. The fact that in most cases of epidermolysis bullosa dystrophica there is a recessive mode of inheritance explains the absence of the disease in other members of the family.

DR EUGENE T BERNSTEIN I am afraid to entertain another diagnosis in the first case, but the condition in the second case impresses me as pemphigus vulgaris. With all respect to the diagnosis made at the Bronx Dermatological Society and with all respect to the histologic examination, I say that in epidermolysis bullosa one often sees involvement of the tongue, and the cystic lesion on the elbow favors the diagnosis of epidermolysis bullosa. The scratch marks are significant. They were produced about ten days ago and at present impress me as a symptom of Kobner's disease. On the other hand, they may be a masquerade for a Nikolsky sign (detachment of the upper layer of the epidermis).

DR FRANK C COMBES It was my impression that in a case of the hereditary type of epidermolysis bullosa a biopsy specimen taken from uninvolved skin would show alterations in the elastic tissue, whereas with the acquired type these alterations occur only in the areas in which the bullae occur. Is that true?

DR DAVID BLOOM In the few cases of my personal experience I have not succeeded in finding elastic tissue absence or deficiency in the normal-appearing skin of these patients. The reports in the literature vary a great deal in regard to this pathologic feature. This is the reason why elastic tissue deficiency cannot be considered as the cause or, at least, as the only cause of epidermolysis bullosa.

DR LOUIS TULIPAN In answer to Dr Bernstein, my case was at first considered one of possible pemphigus vulgaris because of the bullae, but I think that can be ruled out on account of the epidermal cysts. Then again, I agree with Dr Bloom that the condition in this case is really a hereditary dystrophic type, in spite of the fact that it has been called the acquired type. This patient shows epidermal cysts, which is the usual condition in congenital cases. I presented a case here (*ARCH DERMAT & SYPH* 37 22-26 [Jan] 1938) of the dystrophic type in a baby whose entire body was practically covered with lesions and scars and who had lost all the nails. I feel that this patient's condition resembles that one closely except that it is not so generalized. As to the absence or diminution of elastic tissue in the unaffected skin, that varies in different cases.

Parapsoriasis. Presented by DR MAURICE J COSTELLO

H L, a man aged 32, is presented from Bellevue Hospital, complaining of an eruption on the arms, thighs and abdomen of nine months' duration. There is slight itching. The patient applied 10 per cent crude coal tar, without any effect, and then 5 per cent chrysarobin was used until it caused a dermatitis, but the character of the lesions did not change.

Examination shows in the aforementioned areas several well defined, erythematous patches, varying in size from 2 to 5 cm in diameter. There is a fine superficial scaling on the lesions.

Examination of scrapings showed no fungi. Histologic examination showed parapsoriasis.

DISCUSSION

DR HARRY KEIL (by invitation) The case appears to be one of parapsoriasis en plaques, but it should be followed. The ordinary criteria required for this diagnosis are fulfilled, though perhaps there is more pruritus than one would expect. However, I believe that the eventual prognosis in this case is bad.

DR CHARLES WOLF If my memory serves me correctly, articles by Dr Keil give the impression that the diagnosis of mycosis fungoides could be made in the early stages.

DR HARRY KEIL (by invitation) I can point to a case that was presented last month at the monthly staff conference of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, in which the patient showed a typical parapsoriasis en plaques of twelve years' duration, without any infiltration to speak of. Yet a histologic examination showed changes considered typical of mycosis fungoides. The clinical appearance of the eruption, even after twelve years, was that of typical parapsoriasis en plaques. In Dr Costello's case, however, one is dealing with a person who has had an eruption of only nine months' duration. I do not believe it is possible to rule out mycosis fungoides simply because the histologic examination does not show the changes considered pathognomonic of this disease. I pointed that out very clearly in the articles mentioned by Dr Wolf (*ARCH DERMAT & SYPH* (a) 37:465 [March] 1938, (b) 38:545 [Oct] 1938). In my original case three specimens of skin were taken for biopsy, none of which showed the alterations of mycosis fungoides, but four years later (about eight years after onset) another biopsy of skin revealed the typical changes of that disease. I do not want to go into the question of whether mycosis fungoides is such from the beginning, as this question often resolves itself into a matter of quibbling, but the fact remains that there are now available a tremendous number of instances of typical clinical parapsoriasis en plaques that has developed eventually into mycosis fungoides.

DR WILBERT SACHS (by invitation) At the conference mentioned by Dr Keil I made the statement that although the patient's clinical appearance was that of parapsoriasis, the condition was mycosis fungoides from the beginning. Cases with the clinical picture of parapsoriasis microscopically may be either parapsoriasis, and remain so, or mycosis fungoides from the start.

DR MAX SCHEER I think that Dr Keil's case does not bear out Dr Sachs's statement, because his patient for a number of years had no evidence of mycosis fungoides histologically, and it developed only some eight years after the onset of the disease. The whole question, of course, is rather complicated. There is no doubt that cases of parapsoriasis are clinically observed that remain as they are, but there are others which may show mycosis fungoides from the start or which may show it only many years later. I do not think it is correct to assume that in all cases of parapsoriasis the condition is mycosis fungoides, but in a certain number of them this disease develops. That was recognized by Brocq in his textbook (*Brocq, L. Cliniques dermatologiques*, Paris: Masson et Cie, 1927, p 451), in which he reported cases of parapsoriasis which terminated in mycosis fungoides.

DR ISADORE ROSEN I agree with those who say that parapsoriasis may begin as such and terminate as such after many years. There are instances, however, in which mycosis fungoides begins with lesions that resemble parapsoriasis both clinically and histologically and that later show all the clinical features and pathologic changes of mycosis fungoides. It is well known that patients sometimes have psoriasis for many years, the diagnosis having been confirmed by microscopic examination, and then suddenly present both clinical and histologic features of mycosis fungoides. It is difficult to explain this change.

DR PAUL GROSS In several cases I have observed a minor feature which would seem to be characteristic of parapsoriasis en plaques, namely, the evolution of the eruption. The early lesions begin on the distal parts of the extremities, and as the eruption develops, new lesions appear on the thighs and arms and finally on the trunk. Not infrequently this can even be ascertained in taking the patient's history. It would be interesting to hear the experience of the members on that point. Dr Rosen has brought up the fundamental question of mycosis fungoides in relation to parapsoriasis en plaques, as well as psoriasis. One theory is that mycosis fungoides is a lymphoblastoma from the beginning, while more recently the idea has been expressed that benign dermatoses may produce a disturbance of the reticuloendothelial system which is responsible for the lymphoblastic development. When this question is settled, one will be able to make the diagnosis of parapsoriasis en plaques with less hesitation than now, especially after the valuable contribution of Dr Keil.

DR E WILLIAM ABRAMOWITZ I am glad that Dr Gross specified the en plaques variety of parapsoriasis. I do not think the other types of parapsoriasis ever develop into mycosis fungoides.

DR HARRY KEIL (by invitation) With regard to this problem, there are two sets of observations that have to be taken into consideration. First, how did this concept originally arise? The concept was first established on the basis of 3 cases, 2 reported by Unna, Santi and Pollitzer (*Monatsh f prakt Dermat* 10 404, 1890) and 1 by Brocq (*Rev gén de clin et de thérap* 11 577, 1897). Of the first 2, Santi's case turned out to be one of mycosis fungoides, as for the second case, I can only say that Dr Pollitzer told me personally that there was no histologic evidence of mycosis fungoides, but he knew nothing of the eventual clinical course (personal communication, Feb 10, 1937). In regard to Brocq's case, it is little known that this patient had complained of generalized pruritus some two years before the eruption appeared. Moreover, Brocq diagnosed the condition in many subsequent cases as parapsoriasis, but nearly all were later considered instances of mycosis fungoides, proof of this may be found in Civatte's thesis (*Les parapsoriasis de Brocq*, Thesis, Paris, no 216, 1906, Paris, G Steinhil, 1906).

The second consideration is that there are now collected numerous cases of parapsoriasis en plaques that have been observed for twenty years or more. For example, in Savatard's patient mycosis fungoides developed after forty-one years (*Brit J Dermat* 50 150, 1938). The case reported by Gougerot and Burnier is a classic example (*Bull Soc franç de dermat et syph* 41 1528, 1934). I think there will be an increasing frequency of such findings now that these cases are being followed and studied more thoroughly.

Finally, may I add to the records two observations of unusual interest? The first is a quotation from a letter written to me by Dr Udo J Wile (March 30, 1938)

"I am quite sure that I could find from 8 to 12 of my own in which I have been able to see the metamorphosis of parapsoriasis en plaques into mycosis fungoides, and I entirely share your view that whenever I encounter a case of disseminated parapsoriasis it always bespeaks for me a potential lymphoblastomatous development."

In a recent discussion (*ARCH DERMAT & SYPH* 37 117 [Jan] 1938) Dr G M MacKee mentioned the case of a girl afflicted with parapsoriasis that

developed subsequently into mycosis fungoides. In response to my inquiry, Dr MacKee (personal communication, April 9, 1938) stated that the patient was now a grown woman and that the dermatologists who were watching her in Lima, Peru, have also made a diagnosis of mycosis fungoides. This observation is of great interest, for it concerns a case in which the condition had its onset early in the patient's life.

DR MAURICE J COSTELLO The lesions in this case began on the extremities, as Dr Gross mentioned, and spread to the center of the body. It seems to me a rather interesting point that in cases of mycosis fungoides itching is an important feature and is fairly constant, while it is practically never associated with parapsoriasis. Mycosis fungoides responds readily to subfractional (38 r) doses of roentgen rays, and parapsoriasis is resistant and persistent in spite of roentgenotherapy. The lesions of mycosis fungoides are polymorphous and changeable, and those of parapsoriasis are polymorphous and stationary. In view of these facts it is curious that these two eruptions should in any way be related.

Recurrent Symmetric Herpes Simplex of the Fingers. Presented by Dr FRANK C COMBES and DR MAURICE J COSTELLO

T S, a man aged 30, presented from Bellevue Hospital, was previously presented at a meeting of the Manhattan Dermatologic Society (*ARCH DERMAT & SYPH* 39:366 [May] 1938).

The case is presented because of its unusual features of regular seasonal occurrence (in May and October) over a period of fifteen years, in addition to its symmetric location on the fingers of both hands.

DISCUSSION

DR EUGENE T BERNSTEIN I consider this case as one of fixed drug eruption. Has the patient ingested any drugs, such as phenolphthalein?

DR E WILLIAM ABRAMOWITZ I am inclined to agree with Dr Bernstein that this condition is a fixed drug eruption of the herpetic type. The patient on occasion takes a proprietary preparation which is reported to contain acetylsalicylic acid, acetanilid and potassium bromide.

DR MAURICE J COSTELLO The patient states that he has had this eruption for fifteen or sixteen years, and it has recurred in the same locations about four times a year. We have questioned him about drugs, and there is certainly no history of ingestion of any. I gave him six or eight vaccinations with cowpox, and the interval between the last attack and the one he has today is the longest he has ever had in sixteen years, namely, about nine months.

DR HERMAN GOODMAN How many times did the cowpox "take"?

DR MAURICE J COSTELLO There were one "take" and about seven immune reactions, which were represented by a papular reaction which lasted from two to five days.

DR MARION B SULZBERGER Herpetic eruptions confined to the fingers are perhaps not as rare as is generally supposed. They were well described by Dr William Frei (*Dermat Wchnschr* 93:1508 [Sept 26] 1931). The herpes simplex nature of an eruption is usually easy to prove by means of inoculation of a rabbit's cornea. I think that should be done in this case. I should like to point out the fact that because one can recover herpes virus from the lesion does not rule out a fixed eruption. In some cases recurrent fixed localized herpes simplex can occur after ingestion of a certain food or drug, and in such cases one can recover herpes virus, and in these cases there might be a synergistic relation between the virus and the ingested drug or food in producing what is in a certain sense a "fixed" herpetic eruption.

DR LOUIS TULIPAN I think it would be interesting to bring up the question of the effect of vaccination on herpes, as long as it has been mentioned in connec-

tion with this case I believe that physicians who have done any work on this subject should report their results, as some people believe that vaccination is almost the specific treatment for this type of eruption. I have followed this for three years in about 15 cases, and I find that vaccination does little good. It does seem sometimes to increase the intervals between the attacks. Whether it is the effect of the vaccination or not I do not know, but I am sure of one thing: whether one, two or three vaccinations are given and whether the vaccination "takes" or not makes little difference, as the patients get recurrences sooner or later.

DR HERMAN GOODMAN In a long period of observation, the diagnosis of herpes simplex having been made, the patient has been found to give a positive "take" with vaccine obtained from the department of health. This result was not influenced by the history of past vaccination. Repetition of the vaccination within a few days or weeks after a positive "take" has not resulted in secondary positive reaction. There is only one such "take." Until a few months ago when I discussed this question with Dr. Chargin, it was my impression that the patients treated by vaccination had been cured. It is possible that these patients went elsewhere for treatment on recurrent attacks following the vaccination.

DR MAURICE J. COSTELLO We have treated many patients with herpes simplex in private practice and in the clinic. I think in a certain percentage of the cases the vaccination is of no value. In another, smaller percentage, about 40 per cent, it increases the intervals between attacks and decreases the severity and duration of the attacks.

DR HERMAN GOODMAN When I discussed herpes simplex, the diagnosis excluded that due to the ingestion of drugs, such as phenolphthalein.

DR MARION B. SULZBERGER Dr. Wise and I first called attention to our results with this method of treatment in the Year Book of Dermatology and Syphilology for 1934 (Chicago, The Year Book Publishers, Inc., 1934, p. 426). We have discussed smallpox vaccination for recurrent herpes simplex in subsequent Year Books (*ibid.*, 1936, p. 156, 1937, p. 430, 1938, p. 452). I think our statements correspond with those of Dr. Costello. The evidence of the beneficial effects of repeated vaccination seems to be undemable in certain cases of recurrent herpes, at least as far as lengthening the interval between attacks is concerned. I recall particularly the case of one of my secretaries who had recurrent herpes simplex regularly at about monthly intervals. After a series of smallpox vaccinations she had an interval of freedom lasting over two years. After this two year interval the herpes simplex recurrences recommenced, she had attacks at intervals of two or three months, the interval getting shorter each time. I vaccinated her again on three successive occasions, and again there was a remission of a year. I have had a number of similarly successful cases. However, in others I have seen no benefit from vaccination. The question of repetition of vaccination after one has had one "take" is an interesting one. I do not agree with Dr. Goodman. It is true that the "take" with accelerated response signifies a state of allergy to the cowpox virus, but in treating herpes simplex it is not necessarily the state of allergy to pox virus which is significant. Therefore, one cannot assume that the state of allergy to the herpes virus necessarily parallels the sensitivity to pox virus, and one cannot predict from the local result of vaccination—from either the "take" or the "nontake"—what will be the cross immunologic effect on the patient's susceptibility to herpes virus.

DR DAVID BLOOM I have treated with this method only a small number of patients with recurrent herpes, but I have obtained in some of them spectacular results. One of these patients was a girl, a medical student, who was inconvenienced for many years by the monthly recurrence of grouped vesicles over the lumbar and sacral region. Very few vaccinations freed the patient from this eruption for at least one year. Even if this method of treatment is not successful in all cases of recurrent herpes, it is today the method of choice and should be tried in every case.

DR PAUL GROSS The discussion on the treatment of recurrent herpes simplex with smallpox vaccine certainly is interesting, but even the originator of this treatment has not claimed more than 50 per cent of success. As Dr Sulzberger pointed out, there is in use now a substitute and not a specific vaccine. Since there is no other therapy for recurrent herpes simplex, the use of the cowpox vaccine, a simple and fairly innocuous treatment, should not be discouraged.

DR MARION B SULZBERGER I do not think the procedure is entirely harmless and would like to cite an example (not for the record).

DR E WILLIAM ABRAMOWITZ Will Dr Combes and Dr Costello report on this case again, particularly on the results of the administration of a test dose of the proprietary preparation that the patient has been taking? Perhaps the patient will not need the vaccination at all.

Lupus Erythematosus with Involvement of the Palpebral Conjunctiva.

Presented by DR FRANK C COMBES and DR MAURICE J COSTELLO

F C, a woman aged 37, presented from Bellevue Hospital, was previously presented at a meeting of the Bronx Dermatological Society (*ARCH DERMAT & SYPH* 38:671 [April] 1938).

At the present time the eruption, which is erythematosquamous and atrophic, involves the lower eyelids, the chest and the scalp, where there is a palm-sized area of permanent alopecia on the vertex. There is a moderate eversion of the lower eyelids.

The patient was given an intradermal test with old tuberculin in a dilution of 1 to 10,000. A bullous reaction occurred, surrounded by a hand-sized area of erythema and edema, during the existence of which improvement in the eruption was evident. There was also a similar but less severe reaction with a dilution of 1 to 10,000,000. Both reactions can still be seen on the flexor aspect of the left forearm.

DISCUSSION

DR CHARLES WOLF The only point I wish to discuss is the relation between the appearance of the conjunctiva and the disease. If the presenters believe that there is involvement of the conjunctivas, I fail to see it. During involvement of the buccal mucous membrane in cases of lupus erythematosus, superficial ulcerations are seen. Here there is only a mild congestion which is due to the ectropion because of the cicatricial effect on the lower eyelid. Therefore, the inclusion of involvement of the conjunctival mucous membrane is not justified from the appearance. Another point about lupus erythematosus is the response to sulfanilamide therapy in refractory cases. I have used it in 3 patients who have had the disease for many years, and who have cleared up with bismuth therapy and other measures and then had a relapse later. My method of using the drug is the fractional method, giving small doses, of 5 grains (0.32 Gm), three times daily for a week and following this with a rest, checking up, of course, on the blood before and during the treatment.

DR DAVID BLOOM What Dr Wolf just said concerns me, for I presented this patient at this section meeting (*ARCH DERMAT & SYPH* 38:67 [Oct] 1938) just for the purpose of demonstrating lupus erythematosus of the conjunctiva of the lower eyelid. Ulceration is not a necessary feature of lupus erythematosus of the mucous membranes. In this patient not only is the edge of the eyelid affected, suggesting ectropion, but also the inner aspect of the lid, independently of the edge.

DR PAUL GROSS This patient is presented particularly on account of the positive reaction to tuberculin. More recently, Marchionini (*Arch f Dermat u Syph* 158:505, 1929) reported on the results with a Bessau modification of the tuberculin test, and found positive reactions in about 60 per cent of the cases of lupus erythematosus. This percentage has been found rather consistently by other investigators too. Using tuberculomucin many years ago for treatment of different

types of tuberculosis, I also obtained a few excellent results in cases of lupus erythematosus. Even with the advent of sulfanilamide, one ought not to forget the well known fact that lupus erythematosus is a cutaneous manifestation resulting from an infectious focus which may be tuberculous or nontuberculous.

DR E WILLIAM ABRAMOWITZ When there is a positive tuberculin reaction reported in a case of lupus erythematosus there should be an accompanying biopsy to exclude lupus vulgaris of a superficial type. I agree with Dr Wolf in the use of small doses of sulfanilamide in cases of lupus erythematosus, with the accompanying safeguard of blood counts. I use small doses for several weeks and alternate with quinine if the patient can tolerate it. I think this patient presents lupus erythematosus of the palpebral conjunctiva.

DR FRANK C COMBES I agree with those who consider the probability that the tubercle bacillus is either actively present in the lesion in this case or its toxins are responsible for the development of the lesions. This hypothesis is interesting, since the patient improved as a result of the tuberculin test. The reactions were pronounced, with large bullae and considerable infiltration, even with 1 to 10,000 dilution, and a definite reaction was present even with a dilution of 1 to 1,000,000.

DR MAURICE J COSTELLO The patient was presented because of the hypersensitivity to tuberculin. Dr Canizares and I have observed about 10 patients with lupus erythematosus of the discoid type at Bellevue Hospital, who were treated with small doses of sulfanilamide three times a day for many weeks. We think this patient is the only one who showed any improvement.

Unilateral Acneform Eruption Following Bell's Palsy Presented by DR FRANK C COMBES

Y L, a woman aged 19, presented from Bellevue Hospital, was previously presented at a meeting of the New York Dermatological Society on Oct 24, 1939 (*ARCH DERMAT & SYPH* 41 795 [April] 1940).

The condition has been improving.

DISCUSSION

DR EUGENE T BERNSTEIN This patient does not have unilateral involvement. She has also an acneform eruption on the opposite side, but it is more pronounced on the left side where she had the Bell's palsy. Perhaps it is a case of locus minoris resistentiae, meaning the condition is a trophodermatosis, a lessening of the trophic response. She probably has a more pronounced involvement on the one side due to the lesion of the nerve.

DR HERMAN GOODMAN Many cases of petrolatum dermatitis were reported from Germany during the World War, from 1914 to 1918. The preparation the patient said she applied was possibly not the cold cream of the United States Pharmacopeia made with almond oil and sodium borate. The term "cold cream" is applied to any form of grease which has the appearance of being white. This girl may have had dermatitis venenata from the active ingredient in the grease which she applied, with the addition of massage and heat resulting in her present condition.

DR H VICTOR MENDELSON (by invitation) I saw this patient for the first time about four months ago. At that time she presented active acne over the entire left cheek and a few insignificant papules on the right cheek. The predominance of lesions on the left side of the face was so overwhelming that one was justified in considering the eruption unilateral. In my opinion the condition is not dermatitis venenata but acne, the result of a peculiar localized sensitivity caused by the use of a "vibrator" and/or the application of cold cream. This type of cutaneous sensitization is unusual, but it may occur. I recently read a report (Kahn, I S *J Allergy* 10 235 [March] 1939) of a case in which unilateral facial acne occurred after a positive diagnostic intranasal application

of pollen on the same side and reappeared at the sensitized site on four separate occasions in the course of specific treatment when an overdose was given. The patient had had no acne previously, during or subsequent to the period of observation.

DR PAUL GROSS Regarding Dr Goodman's remarks, my own experience with European "vaselinoderma" was that it was due to the fact that the American petrolatum was not available during the years of the World War and the postwar period.

DR FRANK C COMBES Kromayer once stated that the German petrolatum was not fit for any skin. This patient had no dermatitis at any time. I agree with what Dr Bernstein said. She had a mild acne which was aggravated by the Bell's palsy, the massage and the cold cream. Which one of these agents, if any, was responsible it is impossible to say. I imagine it was the cold cream. The left side of her face is now covered with pitted scars, while the right is free. When I first saw her the left side was literally peppered with comedos and pustules.

Scleroderma (Progressive Type). Presented by DR HENRY D NILES

R D, a man aged 26, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complaining of an eruption involving the arms and legs, the face, neck and trunk of one year's duration. The condition started with tight thick skin on the right hand, later on the legs and then on the trunk, face and neck. It is rapidly spreading and becoming worse. On the legs and on the arms, especially on the calves and forearms, the skin is hardened and tight, without inflammatory changes, but shiny and apparently adherent to the subcutaneous tissue. On the periphery of these regions there are erythematous infiltrations, and the progressive stages are visible as smaller, lentil-sized and coalescent white spots. These white spots and slight erythematous changes are present also on the upper part of the chest and back, on the outer sides of the arms and on the neck, also, extending to the adjacent scalp are erythematous changes. In some places there is atrophy beginning with cigaret-paper-like skin. There is generalized lymphadenopathy. General physical examination reveals nothing abnormal except the skin. The blood pressure is 112 systolic and 74 diastolic.

Roentgenograms of the chest were normal. Roentgenograms of the teeth showed slight periapical changes, with alveolar recession and pericemental widening. The Wassermann and Kahn tests of the blood on Nov 10, 1939, showed the serum deeply hemolyzed, and on November 14 there was an anticomplementary reaction, 1 plus. The basal metabolic rate was + 20 per cent. Examination of the urine for creatine gave negative results. Examination of the blood showed 10 mg calcium, 13 mg urea, 24 mg uric acid and 60 mg sugar per hundred cubic centimeters. A blood count on November 11 showed 7,550,000 erythrocytes per cubic millimeter, 114 per cent hemoglobin and 9,400 leukocytes per cubic millimeter, with a differential count of 59 per cent polymorphonuclear leukocytes, 36 per cent lymphocytes, 2 per cent eosinophils and 3 per cent monocytes. On November 15 examination showed 7,350,000 erythrocytes per cubic millimeter, 121 per cent hemoglobin and 7,400 leukocytes per cubic millimeter, with a differential count of 48 per cent polymorphonuclear leukocytes, 32 per cent lymphocytes, 15 per cent eosinophils, 1 per cent basophils and 4 per cent monocytes. On December 15 there were 7,430,000 erythrocytes per cubic millimeter and 138 per cent hemoglobin. There was 70 per cent elevation of the cell volume. The blood volume was 130 cc per kilogram of body weight (the normal being 72 to 100 cc per kilogram of body weight). On sternal puncture there were 78,000 leukocytes and 180 megakaryocytes per cubic millimeter of spinal fluid. Urinalysis gave negative results. Histologic examination showed scleroderma.

by Chambers and Grand (The Chemotactic Reaction of Leukocytes to Foreign Substances in Tissue Culture, *J Cell & Comp Physiol* 8 1 [April] 1936) The injection is made intradermally into the nodule of lupus vulgaris

DISCUSSION

DR OLIVER S ORMSBY Any treatment offering good results in lupus vulgaris should be welcomed This patient had made little progress toward recovery in eighteen years, whereas the starch injection treatment has largely cleared up the condition in ten months

DR ROBERT C RANQUIST (by invitation) This treatment was undertaken because of the startling experience of R L Kile (*ARCH DERMAT & SYPH* 39 471 [March] 1939) The technic is as follows About 0.2 cc of a 15 per cent suspension of arrowroot starch in Ringer's solution is injected into each nodule about every two weeks The explanation offered by Dr Kile is that it was suggested to him because of the positive chemotactic action of starch on the leukocytes The large grain starch molecules, such as those of corn starch or arrowroot starch, are best because they cannot be engulfed by a single leukocyte, and therefore an accumulation of leukocytes takes place at the site of injection Eight months after beginning the treatment this patient's skin is about 80 per cent clear, after her having had the disease for sixty-seven years

Pemphigus Limited to the Mucosa and Conjunctiva Presented by Dr A W STILLIANS

An American woman of at least 50 years said that since 1935 she had had frequent nosebleeds In the fall of 1936 her throat became sore In May 1937 she was seen to have erosions of the mouth, nose, pharynx and larynx which refused to heal under the usual treatment, some would heal and reappear, and others refused to heal The ocular trouble was first noticed early in 1935 In 1937 her blood was tested and the Wassermann and Kahn reactions were found to be weakly positive The Frei test gave a negative result The urine was normal Examination of the blood showed 80 per cent hemoglobin (Sahli method) and 5,500 leukocytes per cubic millimeter, with a differential count within normal limits The blood pressure was 114 systolic and 70 diastolic Between May 1937 and November 1938 the patient was given seventeen intravenous doses of an arsenical and twenty-five intramuscular injections of a bismuth compound These and the potassium iodide always made her feel worse but caused no visible exacerbation of the lesions In November 1938 two phytopharmacologic tests were reported as yielding indexes of 39 and 48 per cent respectively Up to November 1938 the synechiae were limited to the external third of the lower lid Recently the ocular condition has become much worse, although the lesions of the mouth are decidedly better There had never been any blisters on her skin except those from trauma

Examination reveals a well nourished woman whose left bulbar conjunctiva is covered by a milky film up to the limbus of the cornea, there are many adhesions between the bulbar conjunctiva and that of the whole lower lid There is also considerable congestion of the conjunctiva On the inner side of the left cheek is a red macule slightly eroded, and on the anterior surface of the uvula, a triangular erosion with slightly reddened borders There are similar small erosions in the pharynx

DISCUSSION

DR PAUL A O'LEARY, Rochester, Minn, The term ocular pemphigus has also been used to describe contracting conjunctiva of this type, and I have believed for some time that the use of the term pemphigus for this disease was a misnomer The patients rarely, if ever, present the cutaneous manifestations of common or vegetating pemphigus, neither does involvement of other mucous membrane surfaces develop Conversely, this type of conjunctival lesion is not encountered

in the classic case of pemphigus The disease has impressed me as a local infection rather than a systemic one, and continued search for organisms perhaps other than bacteria seems indicated

DR RICHARD S WEISS, St Louis I have observed only 1 case in which the condition began with lesions on the conjunctiva and other lesions proceeded to develop on the body and proved to be pemphigus I am inclined to agree with Dr O'Leary

DR RUBEN NOMLAND, Iowa City I have had the opportunity to observe 6 cases of ocular pemphigus, in 3 of which there were mucous membrane lesions of the mouth and in 2, involvement of the vulva, anus and umbilicus The term ocular pemphigus is well known to ophthalmologists, and it is a syndrome that leads to blindness It is probably different from the pemphigus vulgaris which the dermatologist sees, but ocular pemphigus with lesions of the mucous membranes approaches some of the more benign types of pemphigus vulgaris

DR OLIVER S ORMSBY This subject has come up before this society frequently in the past twenty-five years, and during all this time I have never seen a patient with pemphigus of the skin together with the so-called ocular pemphigus I do not believe that what the ophthalmologists call ocular pemphigus is pemphigus from a dermatologic standpoint. I know, however, that it is a well defined entity I think there is no connection between pemphigus and so-called ocular pemphigus

Atrophoderma with Telangiectasia. Presented by DR OLIVER S ORMSBY

M S, aged 61, was first presented before this society in January 1928 (ARCH DERMAT & SYPH 34.724 [Oct] 1936) The duration of the condition is now forty-seven years At present the entire trunk is involved and shows a patchy, scaly, telangiectatic and atrophic condition Psoriasiform patches are present on the knees and other areas Telangiectasia and atrophy are most pronounced on the breast and on the extensor surfaces of the arms, buttocks and thighs Histologic examination showed a picture compatible with the findings of idiopathic atrophy (Herxheimer) During twelve years' observation and treatment much improvement has occurred on the face and to a more moderate extent on the trunk

DISCUSSION

DR UDO J WILE, Ann Arbor, Mich I recall distinctly having seen this patient before Were it not for the fact that the disease had been present for forty-seven years, I should be suspicious that mycosis fungoides was developing The circumscribed lesions on the legs and thighs, together with the microscopic observation of a sharply circumscribed infiltrate in the upper layer of the corium, certainly suggest this possibility The concept that so-called poikiloderma may be associated with or part of a malignant condition would readily tie up with the idea of beginning mycosis fungoides

DR H E MICHELSON, Minneapolis The microscopic section to me is interesting because in spite of the length of time the patient has had the condition there is still a decided infiltrate I think the condition is acrodermatitis chronica atrophicans

DR PAUL A O'LEARY, Rochester, Minn I have had the opportunity of seeing this patient at previous meetings of this society, and on each occasion the relation of poikiloderma atrophicans vasculare with mycosis fungoides is brought to mind Dr Otto Foerster called attention to the association of these two conditions more than ten years ago Some of my colleagues believe that my concept of poikiloderma is not concrete, however, I have observed this syndrome in association not only with mycosis fungoides but also with chronic lupus erythematosus disseminatus and with dermatomyositis, as well as in its idiopathic form In other words, the cutaneous picture of atrophy and telangiectasia, which is called poikiloderma atrophicans vasculare, either localized or disseminated, may

appear in conjunction with or subsequent to several diseases. So I like to consider poikiloderma atrophicans vasculare as the result of injury to the cutaneous vascular structure by various noxae. I believe a somewhat broader view of poikiloderma should be maintained than that held in the past, and the condition should be considered the end result of the insult of various agents rather than a single entity.

DR EDWARD A. OLIVER. In the case I presented and later reported of mycosis fungoides with poikiloderma-like symptoms, Dr. Nomland first made the diagnosis. It was first presented as a case of acrodermatitis with poikilodermic symptoms.

DR M. OPPENHEIM (by invitation). In a monograph on atrophy of the skin (Finger, E. A., and Oppenheim, M. *Die Hautatrophien*, Vienna, Franz Deuticke, 1910) and in my article in Jadassohn's handbook on atrophy of the skin (Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1931, vol. 8, pt. 2) I expressed the opinion that Jacobi's "Poikiloderma" (*Verhandl. d. deutsch. dermat. Gesellsch.* 9:321, 1907) is only a special form of dermatitis atrophicans. Other cases of poikiloderma are only endings of various cutaneous diseases, as the cases of Petges and Clejat, which are of dermatomyositis, and those of Civatte and Muller, which are of lupus erythematosus. I presented a case before the Vienna Dermatological Society, in which poikiloderma was the prestage of mycosis fungoides. Lichen planus, psoriasis vulgaris and other chronic cutaneous diseases can cause poikiloderma, it may be caused by treatment too. I believe that the presented case is a combination of psoriasis vulgaris with dermatitis or acrodermatitis atrophicans. The clinical findings are in some areas typical for psoriasis vulgaris and in other areas typical for dermatitis atrophicans. The histologic observations are not evidence of mycosis fungoides in the prefungoid stage, because there is no polymorphism of cells. I did not see the conditions of the elastic fibers. If they are absent, then I guess the condition is a combination of dermatitis atrophicans and psoriasis vulgaris.

DR OLIVER S. ORMSBY. I do not think this condition is poikiloderma of Jacobi. In poikiloderma there is always more pigmentation than is present in this case. Some of the lesions here are psoriasiform, but the condition is not psoriasis. These are of comparatively recent origin. The peculiar effect, resembling a roentgen ray burn (healed radiodermatitis), that occurs in poikiloderma is not seen here. The disease is of forty-seven years' duration but has had little effect on the general health. The lesions on the face have practically cleared. The extreme itching is not characteristic of any of the diseases under discussion. The histologic picture is that of idiopathic atrophy. The discussions in this case in the past have centered around idiopathic atrophy, poikiloderma of Jacobi, lupus erythematosus and psoriasis.

Atypical Lepra. Presented by DR S. W. BECKER and DR M. E. OBERMAYER.

The patient was presented at the November 1939 meeting of the Chicago Dermatological Society (*ARCH. DERMAT. & SYPH.* 41:1151 [June] 1940), with a tentative diagnosis of histiocytoma.

The lesions were inoculated with 1 per cent saccharated iron oxide, which was ingested by a few histiocytes but was not taken up by the cells in the massive infiltrate. In sections stained with carbolfuchsin, some but not all of the infiltrating cells were seen to contain a large number of acid-fast bacilli, singly and in groups. Some of the cells contained a large mass of acid-fast material of indefinite form.

On the basis of these observations the diagnosis of lepra has been made.

DISCUSSION

DR UDO J. WILE, Ann Arbor, Mich. While several of the members were examining this patient, I went over various parts of her body with a pin and found that she is completely anesthetic over the entire front and lower extremities. I cannot say why this condition is anything more than the usual leprosy of the mixed type.

DR H M HEDGE I understood Dr Becker to say there was no anesthesia

DR S W BECKER This woman has never had a neurologic examination to my knowledge I did not know that she had anesthetic areas

NOTE—Subsequent neurologic examination revealed hypalgesia over the right side of the face and the upper part of the left side of her back The neurologic consultant stated that the findings suggested involvement of cutaneous sensory nerves but were not convincing

DR UDO J WILE I stuck the pin in both arms $\frac{1}{16}$ inch (0.16 cm)

DR S W BECKER Do you consider this condition an anesthetic type of lepra?

DR UDO J WILE I consider it a mixed type

DR FREDERICK R SCHMIDT I can easily appreciate Dr Becker's quandary, because in 1938 a patient with lepra was presented here whom I had treated for six months for urticaria I then found lepra bacilli in abundance in November 1938, and she was presented later before the society as definitely having leprosy There was no indication of that six months previously

DR DAVID LIEBERTHAL The clinical symptoms are in no respect typical of this disease, and I believe that the painstaking work-up, including the biopsy, made the correct diagnosis possible

A Case for Diagnosis (Dermatitis Herpetiformis? Pemphigus?) Presented by DR THEODORE CORNBLET and DR HERBERT RATTNER

A A, a 73 year old Scotchman, states that he has never had any previous cutaneous trouble He was in good health until May 1939, when one week after moving a mildly pruritic bullous eruption developed over the sternum He broke the blisters and applied sulfur and oil to the denuded areas New crops of bullae appeared on the arms, forearms and thighs, and when the old lesions healed new ones developed He has never been entirely free of any lesions since the onset but has never noticed any in the mouth

The patient's chief complaints on admission to the hospital, on Dec 7, 1939, were itching of the thighs and trunk and constipation

There is no history of any similar disease in the family

Examination of the skin reveals bullae on the extensor surface of the arms and on the flexor surfaces of the upper parts of the forearms, the thighs and the legs, on a nonerythematous base, somewhat grouped and in different degrees of distention, with a translucent amber fluid Several of the bullae contain a milky fluid In the same areas are denuded erythematous lesions of ruptured bullae with some overhanging epidermis and excoriations On the sides of the trunk and abdomen a light pinkish, follicular, papular eruption is present, which was erythematous several days ago but is fading now Physical examination, apart from the skin, gave essentially negative results The skin of the back is erythematous and moist because she has been lying on her back Nikolsky's sign is not present

Urinalysis gave negative results The Kahn reaction of the blood was negative A blood count showed 89 per cent hemoglobin and 4,800,000 erythrocytes and 21,700 leukocytes per cubic millimeter, with a differential count of 68 per cent polymorphonuclear leukocytes, 20 per cent eosinophils, 1 per cent plasma cells, 7 per cent lymphocytes and 4 per cent monocytes Chemical examination of the blood showed normal amounts of nonprotein nitrogen, creatinine and sugar

DISCUSSION

DR. RICHARD S WEISS, St Louis I got the impression that this patient has chronic pemphigus I feel that as time goes on this will become more evident

DR M H EBERT I agree with the presenters that this condition, which at first appeared to be dermatitis herpetiformis, may terminate in pemphigus, but I think at the present time it is dermatitis herpetiformis

DR THEODORE CORNBLEET I felt in the beginning that the distribution of this man's eruption was definitely that of dermatitis herpetiformis, and several of the physicians who saw him feel that that is still the proper diagnosis. There is no question that he has lost considerable ground since he has been hospitalized. I think that there is a lot of room for Dr. Weiss's opinion that this is a case of pemphigus. I believe, however, that at the present time it is impossible to say definitely whether it is pemphigus or Duhring's disease and that it is one of those cases that requires the passage of time before a definite diagnosis can be made.

Recklinghausen's Disease with Demonstration of Nerve Fibers in a Tumor. Presented by DR. M. H. EBERT

H. M., a woman aged 27, presents an extensive eruption which she first noticed at the age of 21. She has 3 brothers and 3 sisters, and no others in the family have a similar trouble. Her intelligence quotient is about normal. The patient is rather undernourished and has a definitely asymmetric face. The cutaneous lesions are most numerous on the trunk and are of four general types: (1) numerous bluish, slightly raised, compressible tumors which give the impression of hibernation on pressure, (2) numerous sessile and pedunculated fibrous tumors varying from scarcely visible growths to bean-sized ones, the color of the normal skin, (3) several café-au-lait macules, and a (4) few walnut-sized, flabby tumors.

The histologic sections demonstrated were taken from a match head-sized fibrous tumor of the second type. Part of the tumor was fixed in Bouin solution and stained with Masson's trichrome stain. Part was impregnated with silver, according to a modified Cajal technic. The sections stained with Masson's trichrome stain show the usual loose fibrillary structure, with numerous nuclei. There are many thin-walled blood vessels and lymph spaces. In the silver-impregnated section there are several cross sections and longitudinal sections of nerve fibers. In the center of the section the nuclei in the reticulum are particularly numerous, and there are many nerve fibrils running between them.

DR. M. H. EBERT The case of Recklinghausen's neurofibromatosis was presented to demonstrate the involvement of the nerve fibers, by means of a modified J. Gay Prieto technic (*Bull. Soc. franç. de dermat. et syph.* 42:1069, 1935) to visualize the finer nerve fibrils with silver nitrate. Von Recklinghausen himself thought the disease consisted of a proliferation of the connective tissue around the intact nerves. Verocay (*Beitr. z. path. Anat. u. z. allg. Path.* 48:1, 1910) years later came to the conclusion that the condition should properly be called a neurinomatosis, because he stated the belief that it was due to the proliferation of the undifferentiated ectodermal cells, which in the course of time would normally develop into Schwann's cells. The section shown today was taken from a small fibroma-like tumor. At the periphery can be seen many normal nerve fibrils, but in the center of the tumor, where the reticulum contains the most nuclei, a nerve fiber is visible which has been much distended, so that the neural axons project out of the neurilemma and run between the nuclei of the surrounding reticulum. This multinucleated reticulum is probably a proliferation of embryonic Schwann cells.

Epidermolysis Bullosa Dystrophica Presented by DR. TIBOR BENEDEK (by invitation)

The patient is a 35 year old man of Irish descent. His parents have been dead for a long time, 5 brothers are living and well. According to the patient's own story, no one in the family has had any cutaneous disease. His present eruption started about twelve years ago. The skin turned purplish on both elbows and knees and became thinner. A few years after the onset blisters appeared within the thinned and purplish areas after bruising the skin.

He was admitted to Mandel Clinic, Michael Reese Hospital, and shows a purplish, atrophic, cigaret-paper-like scarring on both elbows and knees, forearms

and shins. On the left elbow there is a large bulla about 8 by 2 cm, which is tense and filled with clear serum. Around this are numerous blisters, 3 to 5 mm in diameter, tense or flaccid or already ruptured, showing a purplish red, oozing or crusted surface. The left shin shows within the purplish, atrophic areas numerous bullae, 5 to 10 mm in diameter, and further eroded or crusted lesions. Both shins reveal slight pigmentation, hemorrhages and telangiectasis. On the back of the right calf, in an area 12 cm in length, there are partly isolated, partly confluent purplish atrophic lesions. Similar lesions are present on the left calf in smaller number. The skin of both buttocks shows an extensive white, macular, atrophic scarring. On the right buttock there are two larger areas, one 6 by 3 cm and the other smaller. On both shoulders and scattered also on the upper part of the back are similar lesions 10 to 15 mm in diameter.

As accompanying and complicating symptoms there are numerous white macular, atrophic lesions on the chest, the abdomen and along the vertebral column down to the sacrum, they are round, oval or irregular in shape, 5 to 25 mm in diameter. Milium bodies are present, especially on the forearms.

The nails of all the fingers and toes are atrophic, being replaced by a few layers of dirty brownish, horny masses. The hair covering is normal all over the body. The mucous membranes have never shown blister formation, according to the patient. Nikolsky's phenomenon could not be elicited.

NOTE—The Wassermann and Kahn reactions of the blood were negative. Tests showed no hematoporphyrin in the urine. Examination of the blood showed 75 per cent hemoglobin, 4,800,000 red cells and 12,100 white cells per cubic millimeter, with a differential count of 49 per cent neutrophils, 1 per cent eosinophils, 47 per cent lymphocytes and 3 per cent monocytes.

DISCUSSION

DR A. W. STILLIANS. It is a little puzzling as to how to classify this case, because of the ability of the skin to produce bullae only in the atrophic areas. There was a history of atrophy that lasted for several years before the bullae appeared.

Arsenical Keratoses Presented by DR F. E. SENEAR and DR W. K. FORD (by invitation), Rockford, Ill.

Mrs P. S., aged 28, was first seen on Dec. 14, 1939, and complained of horny lesions on the palms and soles of three years' duration. She states that her husband and 7 year old daughter had similar lesions on the palms and soles. Her husband's eruption began three years ago, and her daughter's appeared about ~~one~~ ^{the} year ago. Close questioning failed to reveal any history of ingestion of arsenic or of contact with sprays containing arsenic. The patient was instructed to return with her husband and daughter, which she did on Jan. 4, 1940. At this time her husband stated that there had been a can of powder (used for spraying golf greens) in the basement of their home when they moved into it five years previously, the bottom of the can had gradually rusted away, and some of the contents leaked into their well from time to time, giving the water an acid taste.

The eruptions are strongly suggestive of arsenical keratoses, and the difference in degree of the eruption may possibly be accounted for by the variable quantities of water taken by each patient. Another daughter, aged 3 years, does not present any eruption.

DISCUSSION

DR LOUIS A. BRUNSTING, Rochester, Minn. The presence of keratoses in father, mother and child is remarkable. No doubt these changes are a quantitative response to arsenic rather than an idiosyncratic reaction, such as is suggested when keratoses appear in association with asthma, psoriasis or dermatitis herpetiformis. The investigative work in this case is commendable.

DR OLIVER S ORMSBY All my associates recognized in this patient this afternoon a similarity to one presented a few years ago in whom an arsenical eruption was produced by drinking well water. The patient came from Mexico where he had lived for twenty-five years. He presented a large number of keratoses and several epitheliomas. A careful search was immediately made for arsenic. He stated he had never taken any drugs. Examination of the well water he drank in Mexico showed that it contained a considerable percentage of arsenic. The patient was of interest on account of the extensive distribution and large number of lesions. He was the only member of his family affected.

DR W K FORD (by invitation), Rockford, Ill. There is just one point further that the mother gave as she left the hospital. About a year and a half ago she was in an automobile accident and was confined to the hospital for two and one-half months, and during that time the eruption on the palms and hands cleared up, after her return home there was a recurrence of the eruption.

Kaposi's Sarcoma Presented by DR S J ZAKON (by invitation)

D R, a Jewish man aged 63, was first seen in 1932. At that time he presented a dusky and sharply outlined, infiltrated plaque on the dorsum of the right hand. Histologic examination of the lesion was made, and a diagnosis of Kaposi's sarcoma made. The patient did not return for treatment until October 1939, when he complained of progressing deafness, edema of the legs, swelling of the scrotum and growths in the mouth. Physical examination revealed a generalized, fairly symmetric, discrete eruption involving the scalp, face, chest, back, extremities, roof of the mouth, left tonsil and right auditory canal. The eruption consisted of nodules and plaques, red to plum colored, and boardlike verrucous infiltrations over the dorsa of the feet and ankles. The nodules on the knees appeared to be pedunculated. There were no palpable glands. The lesions of the soft palate and the left tonsil were elevated nodes or tumors, soft and plum colored.

A blood count in October 1939 showed 70 per cent hemoglobin, and 3,730,000 erythrocytes and 6,400 leukocytes per cubic millimeter, with a differential count of 86 per cent polymorphonuclear leukocytes, 8 per cent small lymphocytes, 4 per cent large lymphocytes and 2 per cent monocytes. The blood pressure was 120 systolic and 68 diastolic.

Since October treatment has consisted of solution of potassium arsenite U S P given internally and unfiltered roentgen rays. There is beginning involution of some of the lesions. Histologic examination of lesions from the tonsils and skin showed findings compatible with those usually seen in Kaposi's sarcoma.

DISCUSSION

DR H E MICHELSON, Minneapolis. I thought this case was a remarkable example of Kaposi's sarcoma, but on looking at the patient's fingers, I was struck by the fact that there is a similarity between Kaposi's sarcoma and sarcoidosis, the relation is not definite, but tissues of the same type are prone to react the one in a benign manner and the other in a much more severe manner.

DR S W BECKER. I should like to differ with Dr Michelson because sarcoid involves reticuloendotheliosis, representing a reaction on the part of the histiocytes to some agent which is often known, such as the tubercle bacillus or one of the aberrant forms of the tubercle bacillus. With Kaposi's sarcoma, on the other hand, there is multiplication of cells, multicentric in origin, throughout the body, the stimulus for which multiplication is not known but which results in the formation of a unique type of cell, the fusiform cell. Dr Thatcher and I had occasion to study these cells in tissue cultures (Becker, S W, and Thatcher, H W. Multiple Idiopathic Hemorrhagic Sarcoma of Kaposi, *J Invest Dermat* 1 379, 1938). In these cultures there were many histiocytes which differed greatly from the fusiform cells. The latter were not fibroblasts, and they did not act as malignant cells do. I think that in Kaposi's sarcoma there is a unique type of cell reaction of the embryonic cells. The lymphocytoid cells of Marchand are stimu-

lated by some unknown agent to produce a benign neoplasm. I believe Kaposi's sarcoma is a benign neoplasm. In some instances it goes on to malignant hyperplasia, just as myofibroma of the uterus occasionally goes on to the formation of sarcoma. I do not see how the two conditions, sarcoid and Kaposi's sarcoma, are related.

DR DAVID LIEBERTHAL. The clinical manifestations justify the diagnosis offered. As multiple hemorrhagic sarcoma lasts only a few years and as a rule causes impairment of the general health of the patient sooner or later after the onset of the disease and terminates fatally, Dr Zakon's case may be considered an unusual one, the condition having lasted for about twenty-five years, during which the patient has been enjoying good health.

DR. H. M. HEDGE. In 1920 I presented a case of Kaposi's tumor before the society. The patient is still alive, and I saw him a short time ago.

Avitaminosis. Presented by DR DAVID V. OMENS

L. Y., a Negress aged 35, has been sick for three weeks. She presents an acute and diffuse inflammation of the tissues of the mouth, pharynx, larynx and vagina, with superficial denudation of the epithelium with remnants of the epithelium still intact. She gives a history of having partaken of considerable alcohol with little or no food except some hamburger meat occasionally for some time previous to this condition.

The Wassermann reaction was negative. The urine and the blood sugar content were normal. Cultures for the Klebs-Löffler bacillus were negative. Smears from the mouth revealed Vincent's bacilli, diphtheroid bacilli, staphylococci and streptococci. A vaginal smear was negative for Vincent organisms and monilias. Examination of the blood showed 96 per cent hemoglobin, 5,270,000 erythrocytes and 11,800 leukocytes per cubic millimeter, with a differential count of 75 per cent polymorphonuclear leukocytes, 2 per cent eosinophils, 10 per cent lymphocytes and 13 per cent monocytes. Chemical examination of the blood showed 136 mg sugar, 41 mg nonprotein nitrogen and 24 mg creatinine per hundred cubic centimeters.

DISCUSSION

DR J. R. DRIVER (by invitation), Cleveland. I thought the case was a typical one of pellagra. Treatment with nicotinic acid would probably be specific.

DR J. GARDNER HOPKINS (by invitation), New York. The patient's mouth is filled with ulcerated lesions that look as though they were ruptured bullae. I think pemphigus must be considered.

DR HERBERT RATTNER. I thought that the case was one of pellagra. At the Cook County Hospital cases of pellagra are occasionally encountered with symptoms in the mouth only. And it has been pointed out that one is likely to recover thrush organisms from the mouth of a pellagrin. At any rate, conditions such as the one presented today clear up rapidly when treated with nicotinic acid.

A Case for Diagnosis (Macular Atrophy?) Presented by DR F. E. SENEAR and DR W. K. FORD (by invitation), Rockford, Ill.

A. H., a white girl aged 10 years, is presented. Her mother first noticed the eruption six months ago in the interscapular area. She described it as resembling tiny white blisters that seemed to become solid and grow in size. New lesions appeared from time to time. There were no subjective symptoms. The eruption consisted of discrete round and slightly elevated white macular lesions which were present in the interscapular area, left axillary area and flank, lumbar area and anterior surface of the right thigh.

The patient had whooping cough at the age of 4 years, pleurisy and otitis media at the age of 5 years and varicella followed immediately by measles at the age of 9 years. The eruption did not appear for many months after the last illness.

The blood count showed 81 per cent hemoglobin and 4,230,000 erythrocytes and 7,700 leukocytes per cubic millimeter, with a differential count of 45 per cent poly-

morphonuclear leukocytes, 47 per cent lymphocytes and 8 per cent monocytes. The Kahn reaction was negative, and the urine was normal.

A lesion in the lumbar area was removed for histologic examination. The epidermis was flattened and showed slight intracellular edema. The corium was relatively avascular, with thickening of the collagen fibers, which stained poorly. The elastic fibers were thin and fragmented in the upper part of the corium.

DISCUSSION

DR OLIVER S ORMSBY: It is rather unusual for macular atrophy of that type to occur in a young child. I thought of morphea guttata, and that disease has to be considered. However, the lesions are white, macular and atrophic, which might place it as macular atrophy.

DR M R CARO: In Dr Ford's case the histologic slide showed that the epidermis was flattened, but there was no complete atrophy. The collagen fibers were thickened and hyalinized. Histologically the condition fits in with the diagnosis of white spot disease much better than with macular atrophy.

DR S W BECKER: I agree with Dr Caro that these lesions have a distinctly sclerodermatous appearance. I believe that some of them at least should be placed in the category of scleroderma and perhaps white spot disease, although some of the others may have gone on to atrophy.

DR DAVID LIEBERTHAL: I believe that this case is one of macular atrophy of the skin. It would be desirable to ascertain the family and clinical history, which might be helpful in the interpretation of the case. I have seen and demonstrated before this society some examples which developed on the basis of late papular syphilid.

Macular Atrophy (Schwenninger and Buzzì Type) Presented by DR F E SENEAR and DR IRENE NEUHAUSER (by invitation)

M B, a white girl aged 14, is presented with lesions on the trunk and right arm of many years' duration. She had measles during infancy, which was followed by the appearance of lesions on the trunk. From time to time until the present new lesions have appeared.

The patient has a number of coin-sized, oval and elongated atrophic lesions on the back and the right arm, with the long axis showing a tendency to follow the lines of cleavage. On the lower part of the abdomen there is an irregular, palm-sized area of hyperpigmentation. On the extensor surface of the right arm there are several slightly erythematous, elevated lesions of similar shape and size, which have a soft, doughy consistency on palpation. The atrophic lesions are covered with cigaret-paper-like scars and have a slight tendency toward herniation.

At the time these lesions developed, changes were also noticed in the right eye. The right bulb is slightly enlarged. The pupil is contracted but reacts to light and in accommodation. At present the patient is only able to distinguish light and darkness. Ophthalmoscopic examination revealed atrophy of the optic nerve. The corneal measurements are greater than normal, and the tension of the eye is increased.

A biopsy was not permitted.

DISCUSSION

DR M OFFENHEIM (by invitation): The cases of macular atrophy described by Jadassohn are characteristic. The condition starts as little red spots which become atrophic, with cigaret-paper-like surface. In the last stage there is a hernia-like prominence. Histologically, this hernia-like stage is characterized by fatty tissue in higher layers of the skin than normal. It is a fatty tissue growing in vacuo, substituting the degenerated and diminished connective tissue and elastic fibers of the cutis. The macular atrophy of the Schwenninger-Buzzì type is not a real cutaneous atrophy, it is due to the resorption of the fibromas. Therefore, on palpation one gets the impression, as in cases of atrophie maculosa, of a hole in

the skin. In acrodermatitis tropicans, as the first change histologically is an absence of elastic fibers, they cannot be stained. The reason is a constitutional weakness of the elastic fibers, which is also found in striae gravidarum. For instance, one sees sometimes a pregnant multipara with no striae, whereas sometimes after an abortion striae distensae appear. This girl presents an interesting example of Jadassohn's disease. The girl shown by Dr. Ford had scleroderma, in which the lesions always remain the same size.

**A Case for Diagnosis (Fibrosarcoma of the Shoulder?). Presented by
DR. EDWARD A. OLIVER**

The patient, a Negro aged 50, had a keloid (?) growth removed from the right shoulder in 1932. In March 1935 he was in an automobile accident, at which time he received lacerations of the right shoulder, and the old keloid scar was ruptured. Since then the scar tissue in the areas of multiple lacerations has never healed entirely, being tender all the time and draining occasionally.

General physical examination revealed nothing of importance.

The urine showed a trace of albumin but was otherwise normal. Examination of the blood showed 3,800,000 erythrocytes and 10,000 leukocytes per cubic millimeter, and the hemoglobin was 70 to 75 per cent. The Wassermann and Kahn reactions of the blood were negative. A smear from the lesion showed gram-positive cocci in chains and in irregular groups, no fungus was found.

On Jan. 12, 1940, a blood count showed 3,220,000 erythrocytes and 9,000 leukocytes per cubic millimeter, with a differential count of 78 per cent neutrophils (toxic), 20 per cent lymphocytes and 2 per cent eosinophils, nucleated red cells were present. Histologic examination showed fibrosarcoma of low grade malignancy.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: I cannot reconcile this case and a diagnosis of fibrosarcoma. If a nevus were included in the original keloid, the present condition can well be a melanoblastoma.

DR. EDWARD A. OLIVER: I presented the patient with the diagnosis that the pathologist at the Veterans Administration Facility at Hines, Ill., made, with an interrogation mark, because I was surprised to see the pathologic diagnosis. When I first saw him I thought of the possibility of fibrosarcoma protuberans, as reported by Dr. Andrews some years ago. I also thought of neurosarcoma, though there was little pain.

DR. UDO J. WILE: Fibrosarcoma is ordinarily metastatic.

DR. EDWARD A. OLIVER: The condition is much more malignant than it appears. I showed here some years ago a young man with a lesion on his back, who died about nine months later.

DR. J. R. DRIVER (by invitation), Cleveland: I thought the lesion looked more like fibrosarcoma. There was ulceration present.

DR. F. E. SENEAR: There was much in this eruption suggestive of dermatofibrosarcoma protuberans, since in that condition the lesions often begin with the development of hard cutaneous infiltrate, with later development of the elevated lesions. When the elevated lesions first appear they are likewise often firm, but as the surface becomes eroded they tend to become soft, and such softening is present in some of the lesions here. I have, however, never observed a case of progressive and recurrent fibrosarcoma in which ulceration of the excavation type present in this case had developed.

Myelogenous Leukemia. Presented by DR. F. E. SENEAR

A man aged 44 was well until the fall of 1939, when he complained of fleeting pains in his face. Shortly after this nodules began to develop on the trunk, the face became similarly affected a short time later, and the lips, especially the upper

one, became enlarged. He also complained of soreness of the mouth, which made eating difficult. When he entered the hospital his face showed a typical leonine aspect with numerous large firm red nodules, especially in the supraorbital region. The upper lip was so grossly swollen that it overlapped the lower lip. The skin of the trunk was covered with a great number of firm red elevated nodules varying in diameter from 1 to 3 cm. These were freely movable with the skin and painless. The hard palate showed an extensive ulceration covered with a foul grayish, easily removable membranous slough, and there was severe gingivitis. The posterior cervical, the left supraclavicular and the axillary glands were enlarged. The spleen was enlarged, extending 3 fingerbreadths beneath the costal margin, while the edge of the liver was palpable 2 fingerbreadths beneath the costal margin.

The Wassermann and Kahn reactions were negative. Examination of the blood showed 4,100,000 red cells and 130,000 leukocytes per cubic millimeter, 60,000 platelets, hematocrit (R) 35 per cent and hematocrit (W) 7 per cent. A differential count showed 3 per cent myeloblasts and promyelocytes, 7 per cent neutrophilic myelocytes, 9 per cent neutrophilic metamyelocytes, 16 per cent stab forms, 57 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 1 per cent basophils, 2 per cent lymphocytes and 3 per cent monocytes.

Aspiration of sternal marrow was performed, and the results of the examination of the blood and bone marrow led to a diagnosis of myelogenous leukemia by the hematologists.

DISCUSSION

DR F W LYNCH, St Paul. The eruption is much more extensive than is usual with myelogenous leukemia. Reports of myelogenous leukaemia cutis are more common in recent years, suggesting that this condition may not be as rare as it was once thought but that hematologic study was then inaccurate.

DR J GARDNER HOPKINS (by invitation), New York. I reviewed the reports of myelogenous leukemia of the skin some years ago, and it appeared that all the cases were of atypical leukemia and many, if not all, could be interpreted as monocytic rather than myelogenous leukemia. Of course, the patients did not have enlarged spleen and liver as this man has, neither did they have the same type of cutaneous lesion. I should be interested to know whether the condition was regarded as myelogenous leukemia or as one of the myeloblastic leukemias, about the nature of which there is some argument. This is a most interesting and, I believe, an extremely rare case.

DR UDO J WILE, Ann Arbor, Mich. I have had the opportunity to observe an unusually large number of cases of cutaneous leukemia at the Simpson Memorial Institute at the University of Michigan, an institute founded for the study of diseases of the blood. Experience there has shown that nodules which occasionally precede the other symptoms of lymphatic leukemia occur on the body. Such lesions and infiltrates are far more common in lymphatic leukemia than in the myeloid type. This is with due regard to the fact that lymphatic leukemia is more common.

In myelogenous leukemia the usual form of lesions are hemorrhagic, particularly on the extremities and in the mucous membranes.

When nodules occur in myelogenous leukemia, they have a predilection for the head and face and closely resemble the lesions of nodular leprosy.

Dr Senear's case presents an admirable example of this similarity. The lesions on the skin are like those of nodular leprosy. The hemorrhagic lesions in the mouth are characteristic of the ordinary lesions which occur, particularly near the end of leprosy. If one were to examine microscopically the uninvolved portions of the skin at this stage, I am sure that one would find a cutis infiltrated with cells of the same type as those occurring in the tumor.

DR RICHARD S WEISS, St Louis. I have observed only 1 case, which I can recall, of proved myelogenous leukemia of the skin. It was one Dr Engman Sr had some twenty years ago. The patient had three rather large nodules on the face. They developed before the blood count became abnormal. In the course of two or three months' observation the blood count showed a typical myelogenous

leukemia I have had a large number of cases of leukemia involving the skin, but myelogenous leukemia seems to be extraordinarily rare. The patient presented today shows many more lesions than are usually described in myelogenous leukemia of the skin.

DR F E SENEAR Dr Hopkins has called attention to the fact that pictures of this type are rare in association with myelogenous leukemia, and he asks whether or not the condition may be one of monocytic type. I can say only that the hematology department at the Research and Educational Hospital, University of Illinois, has done a great deal of work on the monocytic type, and in this case the blood picture is reported to be that of a myelogenous type.

A Case for Diagnosis (Lymphosarcoma?). Presented by DR EDWARD A OLIVER and DR LEE KERRIGAN (by invitation)

Mrs G S, a white woman aged 62, was first seen by me on Sept 29, 1936. At that time she complained of a painful tender lesion on the upper alveolar ridge on the left side and a similar lesion on the right side of the soft palate. Both lesions were dark bluish red and had the appearance of lesions of multiform erythema. On being questioned she revealed that she took a pink cathartic pill every night, and it was thought that the pills might contain phenolphthalein. She was given an antiseptic mouth wash and instructed to stop taking the tablets. She improved rapidly, but two months later had a recurrence of the same lesions in the same locations. Five months later the lesion on the right side of the palate was more decided than ever, and a histologic examination showed granuloma. The large lesions finally disappeared, but all during 1937 and 1938 she had continual flare-ups of lesions on both sides of the gums in the front of her mouth. Certain foods seemed to bother her, and she had the material in her plates changed.

By October 1938, two years after I had first seen her, her mouth was not troubling her, but she complained of a "sleepy" feeling in her eyes, and inspection showed a pronounced ptosis of both upper eyelids.

The patient was not seen again for five months, and in February 1939 she returned with severe ptosis of both upper eyelids, together with lipoma-like tumors on both sides of the head in the parietal regions. The Wassermann and Kahn reactions were negative. Examination of the blood showed 4,820,000 erythrocytes and 5,750 leukocytes per cubic millimeter and 91 per cent hemoglobin, with a differential count of 33 per cent small lymphocytes, 6 per cent large mononuclear leukocytes, 57 per cent neutrophils, 1 per cent eosinophils and 3 per cent basophils.

On June 9, 1939, there was a violaceous discoloration of practically the entire top of the head, there was more involvement in the left parietal region than elsewhere, and there were decided alopecia and telangiectasia, with some crusting. A tumor had been removed from the left parietal region, and in the right parietal region another pigeon-egg-like tumor was present. There was still definite ptosis of both upper eyelids. In the right submaxillary region there was a large tumor the size of a pigeon egg. The one that had been present on the left side had been excised. There was moderate enlargement of the axillary nodes.

Histologic examination was made in South Bend, Ind. The following tissues were examined: a small portion of skin from the left parietal region, tissue from under the scalp, an axillary lymph node and a tumor from the submaxillary region. A diagnosis of lymphosarcoma was made.

Since June her treatment has consisted of filtered roentgen ray therapy, as follows:

June 30, 1 skin unit, filtered through 1 mm aluminum to each side of neck

July 21, 1 skin unit, filtered through 1 mm aluminum to right side of neck and left side of scalp

September 1, 1 skin unit, filtered through 1 mm aluminum, to right side of scalp

September 22, $\frac{1}{2}$ skin unit between the eyes and to the right side of scalp

November 15, $\frac{1}{2}$ skin unit to swellings in both parietal regions

On July 13 examination of the blood showed 88 per cent hemoglobin and 4,200,000 erythrocytes and 6,100 leukocytes per cubic millimeter, with a differential count of 73 per cent polymorphonuclear leukocytes, 24 per cent small lymphocytes and 3 per cent large mononuclears

The patient has gained 12 pounds (54 Kg) in weight recently and looks and feels well. She has had wens on her scalp for years, and five of them have been removed at intervals

DISCUSSION

DR F E SENEAR One of the early lesions was of a soft, projecting fungoid type. With regard to the condition of the scalp, I think it is worth emphasizing that this patient had definite telangiectasia as a result of the primary disease of the scalp and that there has been no accentuation of the telangiectasia following the radium therapy.

DR EDWARD A OLIVER I thought this case was fairly interesting, I had never observed one like it. The disappearance of the tumor under small doses of filtered roentgen therapy suggested that possibly the lesion was lymphosarcomatous. The spleen and liver were not palpable when I examined her this morning. Her blood count remains about the same.

A Case for Diagnosis (Dermatitis Herpetiformis in a Child?) Presented by DR F E SENEAR

B S, a girl aged 5 years, noticed a number of vesicles and bullae between the toes which developed in January 1939. Within two weeks similar lesions had appeared on the feet, legs and thighs, within a month the trunk and face were profusely affected and there was a high fever. The child was admitted to a hospital at the time, and a diagnosis of impetigo was made. By October the eruption on the body had cleared, but the lower extremities were still affected. The diagnosis at this time was changed to dermatitis herpetiformis. No details as to the treatments employed were available.

The patient was admitted to the Research and Educational Hospital, University of Illinois, two days ago and at that time showed a bullous and crusted dermatitis about the ears, mouth, neck, chest, back and extremities. Some of the lesions on the extremities were of multiform type and were grouped. The axillary and inguinal glands were considerably enlarged. The child was abjectly miserable. There were 3,880,000 red blood cells and 16,000 white blood cells per cubic millimeter, with 49 per cent lymphocytes, 2 per cent mononuclear cells, 47 per cent neutrophils and 2 per cent basophils.

DISCUSSION

DR UDO J WILE, Ann Arbor, Mich. I think it is difficult in this case to differentiate severe dermatitis herpetiformis from juvenile pemphigus. I prefer the latter diagnosis. A third possibility that would have to be ruled out is that of a bullous iododerma.

DR HOWARD J PARKHURST, Toledo, Ohio. I have seen this patient almost from the onset. Following tonsillitis a bullous eruption appeared on the face and extremities, resembling erythema multiforme. The eruption failed to subside, and in view of the grouping of the bullous and vesicular lesions the diagnosis of dermatitis herpetiformis was decided on. There was eosinophilia, and there was also a large number of eosinophils in the contents of the bullae. The cultures made from the vesicles were negative. She was given an arsenical preparation by mouth and intramuscularly and also a course of injections of whole blood intramuscularly. More recently she has been given vitamins, and for a considerable number of months she was exposed to the sun and more recently to artificial ultra-

violet irradiation. Lately insulin has been administered to stimulate her appetite. The eruption has subsided partially at times but never completely, and she has had recurrent showers of lesions at irregular intervals. The mouth has not been involved. At present she seems to have a new flare-up.

DR UDO J. WILE, Ann Arbor, Mich. May I venture a simple suggestion, that the child's urine be tested for iodine? There are some patients who are so susceptible to small amounts of iodine that they may break out severely from the iodine contained in iodized salt. The members will surely recall the case recorded by Drs. Eller and Fox (*ARCH. DERMAT. & SYPH.* 24:745 [Nov.] 1931) in which a diagnosis of mycosis fungoides was made by some and of various malignant conditions by others and which turned out to be one of fatal nodular iododerma. This patient had not taken iodine in any other amounts than that which is in iodized salt.

DR CLARK W. FINNERUD. You may recall 2 patients that I showed from the Children's Memorial Hospital years ago. The diagnoses of bullous dermatitis herpetiformis were accepted. In neither child was there evidence of appreciable itching. They differed from this patient today in that both responded to large doses of solution of potassium arsenite U. S. P. In both of them there was anything but classic dermatitis herpetiformis. In 1 patient the lesions were clear bullae, in the other there was a pustular element, but both children were high strung and irritable and in this respect gave a different picture from this child today. However, I am inclined to think that the condition in this case is an unusual bullous dermatitis herpetiformis.

DR M. OPPENHEIM (by invitation). The clinical features of the child presented by Dr. Senear remind me of impetigo herpetiformis. This disease occurs mainly in pregnant women and in women after parturition. But there are reports of the disease in men too. In these cases of impetigo herpetiformis a calcium deficiency in the blood was found, and disease of the parathyroid glands was suggested. Administration of parathyroid extract improved the condition and cured it sometimes. I suggest trying parathyroid in this case after the determination of calcium in the blood is made.

A Case for Diagnosis (Lupus Vulgaris Erythematodes, Leloir?) Presented by DR J. R. DRIVER (by invitation), Cleveland

M. M., a man aged 44, who had lived in Russia (Ukraine) until the age of 17, consulted me first in November 1933, complaining of an eruption on the forehead of three years' duration. The eruption at this time consisted of two discrete, irregularly shaped, reddish indurated papules above the left eyebrow, the surface of which was rough and scaly. There were no apple jelly nodules. Diagnoses of lupus erythematosus, tuberculous verrucosa cutis, Boeck's sarcoid and syphilis were considered. The Wassermann and Kline reactions were negative.

Histologic examination of tissue removed showed a thin epidermis, with plugging of the follicles. In the corium there was edema, with thickened collagen fibers. Especially around the hair follicles and deep in the corium there was a dense cellular infiltrate of mononuclear cells, fibroblasts, plasma cells and eosinophils. There were no giant cells.

One treatment with solid carbon dioxide apparently cleared the process for about two years. In February 1936 another similar treatment was given.

The patient was not seen again until May 21, 1937, at which time the lesions on the forehead were practically gone. However, he now complained of "sore patches" on the roof of his mouth of four or five months' duration. Examination revealed an extensive eruption involving the posterior third of the hard palate, the entire soft palate, the uvula, the tonsils, the pillars and to some extent the walls of the pharynx. The process appeared granulomatous, the mucous membrane was thickened and nodular, and patches of leukoplakia covered most of the surface. Histologic examination of tissue removed from the palate revealed the structure of a granuloma, with infiltration of lymphocytes, fibroblasts and plasma cells. There were no giant cells or tubercle formations.

At this time a course of injections of mapharsen was given, without benefit. Light freezing with solid carbon dioxide and acetone and later cauterization with the actual cautery were of only partial, mostly temporary benefit.

In January 1939 the patient was hospitalized for further study. Roentgenograms of the chest were normal, and cultures on sugar-proof mediums were negative. Tissue from lesions on the face and from the mouth was removed again, and the histologic appearance of the cutaneous lesions was essentially the same as that shown previously. Histologic examination of the tissue from the palate showed a stratified squamous epithelial layer, which was covered by a moderately thick layer of keratohyalin. Beneath the epithelium the tissue was densely infiltrated with great numbers of small round cells which had almost no cytoplasm and dense, round nuclei. There were also a few plasma cells and some larger mononuclear cells which had vesicular nuclei. No giant cells were seen, and there were no areas of caseation or tubercle formation. There was a moderate degree of fibroblastic proliferation, and some new blood vessels were formed. No parasites were seen. The pathologists at Lakeside Hospital interpreted the condition as chronic inflammation of the soft palate.

Inoculations of guinea pigs with material from the oral lesions gave negative results for tuberculosis. Examination of the blood revealed 5,530,000 erythrocytes and 4,500 leukocytes per cubic millimeter, with a differential count of 54 per cent polymorphonuclear leukocytes, 35 per cent lymphocytes, 7 per cent large monocytes and 4 per cent eosinophils. An intradermal test with oidiomycin 1:100 (Lederle) gave a positive reaction, with pseudopods. Smears from the palate were negative for tubercle bacilli, yeast, spores and mycelial threads. Serologic tests for syphilis again gave negative results. Physical examination otherwise gave negative results.

Further painting of the oral lesions with a mixture of solid carbon dioxide and acetone produced some improvement. The last treatment was given on July 6, 1939.

A Case for Diagnosis (Lupus Pernio?) Presented by DR. F. E. SENEAR, DR. M. R. CARO and DR. H. C. SCHORR (by invitation)

J. D., a white man aged 50, is presented. Lesions first developed on his cheeks in February 1937. The eruption spread gradually, and by May 1937 the entire face was involved and swollen. The swelling and inflammation persisted all summer but subsided during the following winter. The lesions have persisted since then, with itching and smarting after exposure to the cold and after the ingestion of certain foods, such as eggs, tomatoes, tea and citrus fruits. The lesions are not aggravated by heat or sunshine.

Physical examination shows no abnormalities except those of the skin. Fluoroscopic and roentgenographic examination of the chest showed no evidence of recent or active changes. The urine was normal. The Kahn reaction of the blood was negative. Examination of the blood showed 100 per cent hemoglobin and 6,200,000 erythrocytes and 8,400 leukocytes per cubic millimeter, with a normal differential count.

On each cheek there is a palm-sized, circumscribed, dusky red patch, which extends down to the jaw. Within this there are many pinhead-sized slightly elevated papules. On the chin, root of the nose and top of the nose and forehead there are poorly defined patches of scattered pinhead-sized dusky red soft papules. There are patches with slight dry scaling on the lobes and outer rims of the ears. Diascopic examination shows no apple jelly nodules.

Histologic examination of tissue removed from the lobe of the right ear showed a flattened epidermis, with a moderate amount of intracellular edema. The corium is edematous, with dilated lymphatics and blood vessels. There is a diffuse infiltration of lymphocytes, with fewer histiocytes, and this infiltration is packed more densely about the blood vessels and hair follicles. Acid-fast bacilli were not found with the Ziehl-Neelsen stain.

Lupus Vulgaris Presented by DR DAVID V OMENS and DR WALTER W TOBIN (by invitation)

A woman aged 47 states that she has had an eruption on her face for approximately thirty years. It began with a small area on the right cheek and slowly enlarged until at the present time the entire face is involved. Also, in the past five years similar eruptions have occurred on the upper part of the arms. The disease resulted in scarring, with deformity about the nose. There has been only occasional itching. Approximately twenty years ago a strong solution was applied to the face which seemed to do harm. Since that time she has had irregular treatments with roentgen rays, but to no avail, in fact, the last series of such treatments, six months ago, seemed to her to make the eruption worse.

She is of Nordic extraction and was born in this country. She is married and has had 4 children, and all members of the family save her are free of this disease. Examination discloses a diffuse involvement of the face and a few scattered coin-sized lesions on the shoulders and arms. The eruption consists of a mixture of erythema, scaling, soft, apple jelly-colored nodules and contractile scarring, which has resulted in the beaklike nose and an ectropion of both eyes. The serologic tests of the blood gave negative results, as well as the examination of the urine. Roentgen ray examination of the chest showed no abnormalities. The tuberculin test with a dilution of 1:1,000 gave a negative result, and a biopsy of one of the nodules showed the presence of tubercles with giant, round and epithelioid cells.

DISCUSSION ON PAPERS OF DR DRIVER, DRS SENEAR, CARO AND SCHORR
AND DRS OMENS AND TOBIN

DR H E MICHELSON, Minneapolis. Dr Driver's case is interesting to me because the cutaneous lesions look like lupus vulgaris, but the microscopic section did not come up to my expectations. When lupus vulgaris is progressive it is apt to become hypertrophic, and when it is receding it is prone to be atrophic. I think that application of radium to the lesions of the mouth would be the best treatment.

DR CARL W LAYMON, Minneapolis. Dr Michelson and I have been fortunate in seeing a number of patients recently whose lesions resembled those in the patient presented by Drs Senear, Caro and Schorr. In my opinion, this eruption is a sarcoid. Other eruptions, however, which are clinically similar present a histologic picture which is not consistent with a diagnosis of sarcoid. Some bear more of a clinical likeness to lupus miliaris disseminatus faciei except that the lesions are smaller and more numerous. These have been termed micronodular tuberculids by Pautrier and other French observers, who believe that they are to be closely allied with acnitis except that the lesions do not progress to necrosis clinically and remain tiny nodules. Undoubtedly some cases of such eruptions have been presented under the title of rosacea-like tuberculid, a term which seems to place undue emphasis on the clinical features of another disease entirely unrelated to tuberculosis.

DR S W BECKER. I thought that the microscopic section from the lesion on the forehead in the case of Dr Driver showed lupus sebaceus and that the lesion in the mouth showed round cell infiltration, with no changes in the epidermis, and suggested lupus erythematosus. I saw nothing clinically or microscopically that would suggest lupus vulgaris.

DR PAUL A O'LEARY, Rochester, Minn. When one is obtaining a specimen of skin for biopsy it is advisable to include a piece of normal as well as of pathologic skin. In contrast, when obtaining a specimen of mucous membrane for biopsy, the material should be excised from the center or middle of the pathologic process rather than from the periphery. This is especially true in lesions of the tongue where the surrounding inflammatory reaction is usually intense and might explain the absence of tubercles in the sections from the lesion in Dr Driver's patient.

DR LOUIS A BRUNSTING, Rochester, Minn. The appearance of the face recalls to my mind 2 patients whom I have observed who presented a diffuse

erythema of the face, with miliary nodules suggesting lupus miliaris follicularis. Microscopic examination, however, revealed evidences of disseminated lupus erythematosus plus deeper foci with the infiltrative structure of sarcoid. This combination is decidedly unusual.

DR CLARK W FINNERUD: In regard to Dr Driver's patient, I expected to find a histologic picture of lupus vulgaris and was surprised to find characteristic changes of lupus erythematosus.

DR M OPPENHEIM (by invitation): I believe that one must consider rosacea in Dr Senear's case. I think the condition is rosacea due to exposure to low temperatures. The symmetric involvement of both ears and the absence of typical scars, without infiltration, suggest to me rosacea with permosis.

In Dr Driver's case the clinical diagnosis does not seem to be completely confirmed by the histologic observations. The clinical features are those of lupus vulgaris.

DR OLIVER S ORMSBY: My conception of lupus pernio is based on a study of many patients. There are two distinct conditions described under this title. Lupus pernio, described originally by Hutchinson, eventually terminates in lupus erythematosus. In its early stages there is an erythematous eruption on the face, nose and ears that varies in activity for a period and finally becomes permanent and is then typical lupus erythematosus. In the early and more transient stage the lesions resemble chilblain. Lupus pernio of Besnier, which is now considered sarcoid, is a condition in which there is a condition of lesions, erythematous nodules and plaques on the face, fingers, hands and toes. Sometimes they break down and ulcerate, or they may be absorbed, leaving atrophy. On diascopic pressure brown nodules remain. This type is therefore tuberculous, whereas lupus pernio of Hutchinson is lupus erythematosus. I should consider this case of Drs Senear, Caro and Schorr not as one of rosacea but rather as one of some form of tuberculosis.

DR H E MICHELSON, Minneapolis: I think it is a good rule in dermatology never to diagnose against positive evidence. Since the patient presented by Drs Senear, Caro and Schorr has polycythemia, it is a bit bold to venture another diagnosis. Had I not known of this condition of the blood, my first thought would have been sarcoid. The microscopic section did not give me any particular lead, and I think that further biopsies of tissue from various areas will have to be performed before it is possible to make a decision.

DR F E SENEAR: It was long after encountering the case that we became aware of the polycythemia that was present.

I agree with Dr Ormsby that this condition cannot be considered rosacea, even of severe degree, one reason being the distinct evidence of atrophy in the flush areas of the cheek. I felt that there was definite atrophy here. We shall try to follow Dr Michelson's suggestion and get another specimen for biopsy, because Dr Caro said that the specimen we had was not taken sufficiently deep to be satisfactory.

Liposarcoma Presented by DR FREDERICK R SCHMIDT

H P, a white man aged 50, was first seen on July 25, 1939, suffering from an ulcerated mass on the neck of several months' duration. He did not remember having a lump there previously. The hardness of this tumor suggested actinomycosis, but no actinomyces were found.

Covering the anterior chest wall and the clavicle were 5 hazelnut-sized, elevated, hard, smooth nodes. The Wassermann reaction of the blood was negative. The blood picture was suggestive of leukemia, there were 100,000 leukocytes per cubic millimeter, chiefly mature polymorphonuclear leukocytes.

The patient died three months later, but an autopsy was not performed.

Tissue removed from the mass in the neck and the tumor of the skin histologically showed the presence of large cells scattered singly and in groups through-

cut the section. These large cells contained detritus. Their cytoplasm was granular, and the nuclei were situated in the center and at the periphery. The cells were surrounded by strands of reticulum. The large cells showed fat droplets when stained with sudan III.

Adenoma Sudoriferum Presented by DR. FREDERICK R. SCHMIDT

L. J., a white woman aged 69, came to the Grant Hospital in May 1939, with a small tumor of the right hip. This had appeared three years previously and had gradually grown in size to 3 cm. in diameter. It was skin colored, slightly elevated and freely movable in the skin.

Examination of the gross specimen showed that the epidermis was thinner. Filling the entire corium was a more or less sharply circumscribed area composed of cells arranged singly and in groups between fasciculi of connective tissue. These cells, many of which were arranged as alveoli with a central lumen filled with a homogeneous material, were cuboidal, with a small, darkly staining nucleus, resembling in structure those of a mature sweat gland. Differential staining with Masson's trichrome, aniline blue and with a Nile blue sulfate stain clearly showed the characteristics of a sweat gland.

NEW YORK DERMATOLOGICAL SOCIETY

FRANK C. COMBES, M.D., *President*

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Jan. 23, 1940

Eczema Simulating Lymphoblastoma (Mycosis Fungoides). Presented by DR. EUGENE F. TRAUB

D. S., a man aged 42, is presented from Welfare Hospital, Welfare Island. The patient's father and a cousin suffer from asthma, a sister has hay fever, and a cousin has eczema of the hands. The patient's eruption began in March 1937, one week after an attack of coryza. The first manifestation was itching and dryness of the skin of the right leg and then of the entire body, followed by cracking, scaling, elevated, erythematous patches. The patient was treated with linseed oil, solution of calcium hydroxide, U. S. P. and sun baths, and the eruption had cleared up by May 1937. On being tested, he was found to be sensitive to spices. In September 1937, after a coryza, generalized itching developed, and then red papules appeared over the back. The skin cleared up entirely after two weeks in Florida, but when he returned to New York the itching and red plaques recurred. The condition remained in a severe state until September 1938, when it improved briefly with sun baths. Two injections of milk are said to have "caused the skin to break out in all kinds of blotches." "Extraction of infected teeth caused purulent discharge from the legs." Histologic examination at Kings County Hospital in 1938 was reported as showing mycosis fungoides.

Examination shows a thickened lichenified eruption, with generalized plaque-like disks, and scattered individual discrete papules, including lesions on the glans and shaft of the penis.

The patient's maximum and minimum weights have been 182 and 126 pounds (82.6 and 57.2 Kg.), respectively. His present weight is 136 pounds (61.7 Kg.). Urinalysis gave negative results. A blood count showed 4,200,000 erythrocytes per cubic millimeter, 80 per cent hemoglobin and 7,500 leukocytes per cubic millimeter, with 55 per cent polymorphonuclear leukocytes, 43 per cent lymphocytes and 2 per cent monocytes.

Histologic examination showed slight acanthosis. There was an occasional degenerated epithelial cell in the corium. In the upper third of the corium, including the papillary layer, there were small collections of leukocytes arranged in nodules and streamers. Some of these were perivascular. The majority of these cells were lymphocytes and mononuclear leukocytes. There were a moderate number of plasma cells and occasional polymorphonuclear leukocytes and eosinophils. An occasional mitotic figure was noted in these focal collections of cells. There were some connective tissue condensation and slight edema of the papillae. The foci of inflammatory cells were small and not particularly numerous. A diagnosis of chronic inflammatory reaction of the skin was made. The lesions showed several criteria of early lesions of mycosis fungoides.

The treatment during his present hospitalization has been the removal of as many foci of infection as possible, injections of typhoid vaccine, the application of many local ointments and lotions and three treatments with roentgen rays.

DISCUSSION

DR J FRANK FRASER. I disagree with the pathologist who made a diagnosis of mycosis fungoides on the basis of the microscopic findings. I also disagree with the clinicians who made that diagnosis. I cannot see any features of mycosis fungoides in the slides which the presenter has exhibited. In regard to the clinical picture, in my opinion there is not a single feature in the gross appearance of the lesions that would lead me to consider the diagnosis of mycosis fungoides. I agree with Dr Traub that the condition in this case is chronic eczema.

DR EDWARD R MALONEY. I agree with Dr Traub's clinical interpretation in this case.

DR GEORGE C ANDREWS (by invitation). The condition looks like eczema of internal origin, and I suggest looking for focal infections, especially in the teeth, and perhaps giving the patient sulfanilamide.

DR GEORGE MILLER MACKEE. I also am unable to accept the diagnosis of mycosis fungoides on the basis of anything I saw in the patient or under the microscope. Under the microscope there is a perivascular infiltration, for the most part of lymphocytes, with a number of eosinophils. From my rather hasty examination I could see no evidence of granuloma and certainly none of mycosis fungoides. At the same time I think that any eczema that lasts for years and is more or less generalized and even somewhat intermittent must be considered as a possible potential mycosis fungoides. There are many patients who have been treated for eczema for years and occasionally for psoriasis and are finally found to have mycosis fungoides. With this variety of eczema the discoid lesions constitute a prominent feature, and pruritus is severe, but lichenification, allergy and atopy are not so manifest as with neurodermatitis. This variety might be called discoid eczematoid dermatitis.

DR A BENSON CANNON. I am convinced of the diagnosis of dermatitis with lichenification due to a sensitization, most likely to some local irritant. I reported 8 such cases at the meeting of the American Dermatological Association in June 1938 (*ARCH DERMAT & SYPH* 39 846 [May] 1939), in all of which I found that there was a history of allergy either in the families or in the patients themselves. Several of my patients reacted to pollens and several to drugs. In 3 patients an onset of asthma or urticaria followed by the characteristic dermatitis appeared after the use of a local irritant, in 1 case it was coal tar, in another, chloroform, and in a third, pyrethrum. Invariably patients suffering from this type of dermatitis, simulating at times a disease of the lymphoblastoma group, were greatly benefited or cured by a change of climate. I have some 35 patients who have suffered from the disease for years and who have been cured by going to Hot Springs, N Mex, or to Texas, Arizona, California or Florida. Occasionally such a sufferer will get well by going to a northern climate. It sometimes happens that a patient may have to change to one or more sections of the country before he

becomes free from the condition I saw 2 patients, who had spent about ten years in hospitals in various parts of the country, become well in a few weeks after arriving at Hot Springs, N Mex., and they have remained so for three years while engaged in work in El Paso, Texas I have just had 2 patients suffering with the same type of dermatitis become well within a week to ten days after taking sun and ocean baths in Florida They broke out with a violent attack of the condition four days after coming back to New York The patients on reaching a southern climate almost invariably describe a feeling of mental and physical relaxation, freedom from itching and a rapid clearing up of their skin Regardless of what one's view may be of these varied, distressing symptoms, one cannot avoid the inference that environment plays a vital role in the production of the lesions, and the only cure that I know of is a change of climate, more often to one with warm sunshine

DR HOWARD FOX I agree with the members who do not consider this case to be one of mycosis fungoides The eruption is generalized, symmetric and profuse, which speaks against this diagnosis There are also many scratch marks, which are seldom seen in patients with mycosis fungoides In spite of the fact that the disease causes severe itching, the patient rarely tears the skin with the finger nails Finally, in my opinion, the individual lesions do not look like those of mycosis fungoides There is no variation in infiltration in different lesions or in different parts of the same lesion, such as is often present in patients with mycosis fungoides I agree entirely with what Dr Cannon said about climate and have advised numerous patients with obstinate generalized eruptions to visit, or if necessary to live in, a warm climate, such as that of Arizona, Florida or southern California

DR PAUL E BECHET I agree with those who are against the diagnosis of mycosis fungoides One of the excellent reasons advanced against that diagnosis is the enormous number of lesions present Mycosis fungoides does not usually present the multiplicity of lesions this patient exhibits On the other hand, he presents the common picture of generalized itching eczematoid dermatitis, which is seen so frequently in the hospitals

DR FRANK C COMBES I agree with the diagnosis of chronic discoid and lichenoid dermatosis for the reasons which have been stated, and I do not think this man will get well until he is sent away He might get some temporary improvement from heat therapy, but I think any improvement will be temporary

DR JEROME KINGSBURY I agree with all the previous speakers that the case is not one of mycosis fungoides I can imagine, however, that at times some of these lesions may have presented an appearance that would have warranted a consideration, temporarily at least, of that diagnosis

DR EUGENE F TRAUB I should like to add only one or two points In the first place, I am delighted that my interpretation, despite the fact that the histologic report from two hospitals was of mycosis fungoides, was accepted by the members After all, the one thing that would exclude the diagnosis of chronic discoid and lichenoid eczema would be a definite histologic picture of mycosis fungoides Dr Fraser's opinion, on examination of the section, that this condition is not mycosis fungoides rules that out The second point I want to make is that in this type of case there has always been a decided difference of opinion as to whether or not the patient is allergic to something This patient comes from a family with a definite history of hay fever and asthma, and he has been found to be sensitive to a number of things That, of course, would not exclude a diagnosis of mycosis fungoides Dr Cannon has repeatedly emphasized that point, but it is contrary to the experience of Sulzberger and Garbe (*ARCH DERMAT & SYPH* 36 247 [Aug] 1937) In their 9 cases, they reported no history of allergy in the family, and the patients were not sensitive to cutaneous tests In some of the cases that have been under my observation I have felt that there was a definite allergy to bacteria or fungi and, in some, an environmental allergy A point that made me feel that the condition in this case was not mycosis fungoides

was that there were areas of healthy skin between the lesions. Also, this eruption was in no way configurate, with the horseshoe-shaped and eccentric lesions typical of mycosis fungoides. That picture, together with the lesions on the penis, which are unusual in mycosis fungoides, although they could occur, make me feel that clinically the diagnosis of mycosis fungoides can be ruled out.

Recurring Erythema Multiforme Associated with Pregnancy Presented by DR JEROME KINGSBURY

E C, a woman aged 36, married, has a daughter, now aged 15, by her first husband, and 4 other children, aged 4, 3, 2 and 1 years, by her second husband. She has now been pregnant four months. During all her pregnancies of the past five years the patient has had a generalized pruritic eruption. The eruption began as a rule within the first three months of the pregnancy and did not clear up until after delivery. There is a history of syphilis, with a considerable amount of treatment about fourteen years ago. The Wassermann reaction now is negative, and all tests in recent years are said to have given negative results. The present eruption has been active for the past three months. It is inflammatory and involves the trunk, the neck and the extremities. The lesions are large and elevated, with a tendency to circinate arrangement. There are no vesicles or pigmentation.

DISCUSSION

(The members agreed unanimously with the diagnosis as presented.)

Recurrent Painful Ulcerations of the Lower Lip Presented by DR JOSEPH J ELLER

N B, a man aged 52, is presented for Dr Lloyd H Kest. Examination eight months ago showed that the lower lip was scaly, fissured and crusted, with pigmented areas. The patient gave a history of having had this condition more or less for two and one-half years. He was under treatment by various physicians. At times there was almost a complete disappearance of the lesions, but at no time were they entirely gone. The ulcerations are painful.

The patient states that he had an appendectomy twenty years ago, followed two years later by an operation for a varicocele. Eight years ago a routine Wassermann test of the blood gave a 4 plus reaction. The patient knew of no sore on the penis or other eruption on the body previous to the present condition. He received continuous treatment for over two years for the positive Wassermann reaction, followed by intermittent treatment for four years. Two Wassermann reactions during the past few years were negative, but an examination two days ago gave the following results: cholesterol antigen, 4 plus, crude antigen, 1 plus, Kline test, 3 plus, and Kline diagnostic test, negative.

On examination today there are no signs of ulceration, crusting or scaliness on either the upper or the lower lip. The lower lip, however, is pigmented in some areas and shows a thinning of the mucous membranes, particularly on areas previously ulcerated.

During the past three years the patient has been treated by different dermatologists and has received roentgenotherapy, local applications of wet dressings and various salves and intravenous injections of gold and sodium thiosulfate and bismuth subsalicylate. The patient has been limited to the use of bland mouth washes, has abstained from drinking alcoholic beverages and smoking, and has not used any irritating lotions or remedies on his face after shaving. Microscopic and cultural examinations for fungi gave negative results. The buccal mucous membranes showed superficial whitish striations resembling somewhat lichen planus.

The following diagnoses were considered: drug eruption (this has been ruled out), dermatitis venenata, allergy, lupus erythematosus, some fungus infection, cheilitis (in connection with light sensitivity) and lichen planus erythematosus.

The patient responded best to applications of a bland emollient such as white petrolatum, and alternating injections of gold sodium thiosulfate, later alternating with a bismuth compound. He was also given vitamin B complex by mouth. Despite satisfactory improvement, there have been recurrences under this treatment.

DISCUSSION

DR A BENSON CANNON I suspect lichen planus. The white, lacy membranes covering the cheeks are characteristic of that condition. The slight, warty thickening in the center opposite the second molars on the right cheek may also be found in cases of lichen planus. The outline of the lip lesion with the raised threadlike border and scaly center may also be lichen planus. The telangiectatic blood vessels in this lesion suggest excessive irradiation.

DR EUGENE F TRAUB Naturally it is difficult to make a positive diagnosis in a case like this on first inspection. It is my opinion that the lesion on the right buccal mucosa, although it certainly looks like lichen planus, is perhaps not the most characteristic part of this eruption, the lesion on the left side of the dorsal surface of the tongue and the one on the lip which extends from the right buccal mucosa in one continuous plaque on to the vermilion border of the lip are the most characteristic. While I have not frequently observed leukoplakia extending out on the vermilion border of the lip, nevertheless I think this diagnosis is more likely than lichen planus or lupus erythematosus. The fact that the patient has had syphilis also seems to favor the diagnosis of leukoplakia.

DR FRANK C COMBES I agree with what Dr Traub has said about the diagnosis in this case being leukoplakia. There are large, apparently rough plaques on both cheeks, particularly the left one, extending on to the upper lip on the left side. The patches further back along the mucosa are suggestive that this man may bite the oral mucosa there with his teeth. The whole thing looks to me like leukoplakia plus the traumatic lesions.

DR GEORGE MILLER MACKEE The patient told me that at times the lip was absolutely normal. If that is so, I do not think the condition can be leukoplakia. Lichen planus and lupus erythematosus must be considered.

DR JOSEPH J ELLER The man at times had definite ulcerations, with bleeding, crusting and extreme pain, so that he was conscious of it all day and even had trouble sleeping at night. The lesions would break down without any trauma. After healing, the lesions would glisten with a thin epithelial layer over the previously ulcerated areas. The condition looks better today than it has in the six months I have had him under treatment. He improved under treatment with alternating intravenous injections of gold and sodium thiosulfate and a bismuth compound. Does any one think the condition might be lupus erythematosus?

DR EUGENE F TRAUB Regardless of the history, the lesions on the tongue seem to me to be leukoplakia without doubt. The ulceration which comes and goes may be, and not infrequently is, a part of leukoplakia.

A Case for Diagnosis (Dermatophytosis of the Keratotic Type?) Presented by DR HOWARD FOX

A F, a bill poster aged 43, was referred from the Veterans Administration Facility. Two years ago an epithelioma was removed from the center of the lower lip. He now presents a dime-sized patch of leukoplakia adjacent to the scar on the vermilion border of the lip.

For the past six years he has had patches of keratosis on the palms and soles. They are sharply defined, greatly thickened, yellowish white verrucous areas. Those on the soles are somewhat tender and cause pain on walking. Many of them have a reddish areola. On the palms the lesions are present on the hypothenar eminences, the largest being 2 inches (5 cm) in diameter. There is also a small patch on the radial side of the right index finger. The eruption on the sole is more profuse and is present on the bearing surface of the toes, the

balls of the feet, heels and parts of the center of the soles, the patient being rather flat footed. The finger nails are normal, but the toe nails are considerably thickened, opaque and yellowish and show moderate elevation of the distal parts above the nail bed. There is considerable hyperhidrosis of the palms and soles.

The patient previously suffered from Dupuytren's contraction, which was successfully treated by 1000 röntgen rays. During this treatment the patches on the hypothenar eminences were also irradiated and disappeared temporarily but recurred at the end of three months. The patient shows patches of typical vitiligo on the backs of the hands.

He states that the paste he uses in his work consists solely of starch and water, and that he usually prepares it himself. He gives no history of arsenical or other medication. Examination of the urine, before and after intravenous injection of sodium thiosulfate, showed no arsenic. The patient states that he has never had gonorrhea. He has no stricture of the urethra, the complement fixation test for gonorrhea gave a negative reaction, and no gonococci were found in the prostatic secretion. He has never had any swelling or pain in the joints. A general physical examination showed no abnormality. A microscopic examination of scrapings from a lesion on the sole showed a small amount of mycelium. The trichophytin test gave a negative reaction.

DISCUSSION

DR A BENSON CANNON. I have never seen lesions such as this man presents other than in cases of psoriasis, and had Dr Fox not told of finding the fungus of ringworm in scrapings taken from the scaly areas, I should have diagnosed the case as psoriasis.

DR EUGENE F TRAUB. My impression was that this patient had a rather unusual psoriasis, and I suggest that a biopsy be performed to exclude or confirm that diagnosis. The finding of fungi would not necessarily exclude the diagnosis of psoriasis, because it is possible to find fungi in lesions that are not due solely to ringworm. I recall a patient with tertiary syphilis who presented a squamous eruption on the sole in a configurate pattern suggesting a tertiary lesion, the Wassermann reaction being 4 plus, and fungi were found in the lesion. The fact that the trichophytin reaction was negative would not rule out the diagnosis of a fungous infection, because in a fair percentage of cases, up to 20 per cent, the regular twenty-four to forty-eight hour reading of a trichophytin test may be negative even when fungi have been found or a dermatophytid has been present. This has been recorded by a number of observers. Therefore, it appears that in this case there are two possibilities which have not been ruled out.

DR GEORGE MILLER MACKEE. My tentative diagnosis would be psoriasis of an unusual type. I agree with Dr Traub that a negative result of a trichophytin test does not rule out dermatophytosis, but I do not agree that it does not rule out dermatophytid. I doubt if there can be a dermatophytid with a negative trichophytin reaction. I agree with Dr Traub that a fungus may be a saprophyte.

DR J GARDNER HOPKINS. I have never seen hyperkeratoses like these in cases of psoriasis. Whether such lesions can appear at this time of life, I do not know. They are perfectly symmetric, and the horny formations like stalactites hanging off the toes are most striking. One sees pictures of them in cases of Hong Kong foot, which is a fungous infection. The only ones I have seen were in cases of congenital keratoderma or ichthyosis hystrix.

DR GEORGE MILLER MACKEE. The toe nails are badly involved too. They could be evidence of either psoriasis or onychomycosis.

DR HOWARD FOX. I should like to know Dr Cannon's opinion about arsenic as a possible cause of this eruption.

DR A BENSON CANNON. I believe that two types of arsenical keratosis are recognized, the more common one consisting of horny plugs on the soles and palms which sometimes undergo epitheliomatous changes. This type of keratosis

is usually found in patients who have been taking solution of potassium arsenite $U S P$ or arsenic trioxide $U S P$, while the other type is the uniform hyperkeratosis of the soles and palms, symptoms seen after ingestion of arsphenamine. Occasionally one may find a combination of the two types of lesions in the same patient. Sometimes one may be aided in the diagnosis of palmar and plantar keratosis due to arsenic by the finding of eczematized areas in other parts of the cutaneous surface or of brown pigmented areas of skin. I believe that the absence of arsenic in one's urine does not necessarily mean that the patient has not a retention of arsenic. One may find large quantities of arsenic in the blood and none in the urine. When arsenic is found in the urine, it is usually thought that the patient is excreting the metal and probably will eventually eliminate the drug from his system.

DR HOWARD FOX: I felt reasonably sure that both gonorrhea and arsenic could be excluded as causes of the keratoderma in this case. I also felt that the diagnosis of hereditary keratoderma was improbable. The two most likely possibilities seemed to be the keratotic type of fungous infection and psoriasis. The changes in the toe nails could be present in either of these conditions.

Bromoderma with Peculiar Purpuric Lesions Presented by DR PAUL E BECHET

T. A., a woman aged 32, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, states that her eruption has been present for eight months and that it appeared several weeks after the administration of elixir of three bromides $N F$ for nervousness. Since that time she has taken the drug at intervals. The lesions consist of "shotty" dark red papules and pustules scattered over the face, trunk and extremities. The purpuric lesions are not different from the ordinary simplex variety and can be seen on both the legs and the arms, particularly about the knees and elbows.

DISCUSSION

DR HOWARD FOX: This picture is not the ordinary one of acne due to bromide, in which the lesions are somewhat tender papulopustules. These are small, flat, indolent papules. However, as the patient has been taking bromides for the past eight months I think a bromoderma should be considered.

DR GEORGE MILLER MACKEE: I suppose that diagnosis can be accepted tentatively, but it seems to me that the eruption on the legs in addition to being purpuric is also erythematous and could be classified as erythema multiforme or erythema toxicum. Eruptions of that sort can be caused by various drugs, but rarely by bromides, although it is possible for bromides to do it. The possibility of a coincidence must be considered. The condition may be erythema multiforme in a patient who happened to be taking bromides. The acneform lesions do not seem to be numerous enough to make one sure that the condition is due to bromides. The diagnosis of bromoderma is at least doubtful.

DR EUGENE F. TRAUB: I agree with what has been said, especially about the purpuric lesions. In looking over the literature about bromoderma, I do not recall that purpuric lesions were ever a part of the condition. The patient states that the condition appeared relatively recently on the legs, and as nearly as I could make out, it followed the taking of several tablets of acetylsalicylic acid and some other remedy which her physician had prescribed for a cold. It may, therefore, be a dermatitis medicamentosa but due to some remedy other than the bromide.

DR FRANK C. COMBES: I doubt that this condition is bromoderma, for the reasons Dr. Fox has stated. The lesions are not nearly inflammatory enough, nor are they tender. I feel that further study and observation are needed in this case before the blame for the eruption can be put entirely on bromides.

DR PAUL E BECHET To my mind the acneform lesions on the face are definitely due to the bromides. They are characteristic. They are rather hard and discrete, with no evidence of seborrhea, comedos or pustules. Therefore, the lesions on the face conform, according to my experience, to the typical acne occurring after prolonged ingestion of either member of the halogen group. As for the question of purpuric lesions in cases of bromoderma, I have never observed a case, but it seems plausible to assume that the two conditions are allied. In 3 cases of iododerma observed some years ago, there were purpuric and even hemorrhagic and gangrenous lesions. Therefore, I do not see why one cannot observe hemorrhagic lesions in cases of bromoderma, and I am under the impression that there are reports of it. The patient gave me a different history from the one given to Dr Traub. She said the entire eruption occurred a month after she took the bromides.

Epidermolysis Bullosa Acquisita Presented by DR PAUL E BECHET

L. M., a woman aged 43, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in December 1939, for relief of a severe bullous eruption of one year's duration. The lesions consist of large vesicles and bullae, particularly numerous on areas exposed to trauma, such as on the hands and legs. The patient states definitely that bullae arise within twenty-four hours after a scratch or a bruise. A large bulla developed on one tibia after she struck it against the bath tub the previous day. The buccal mucosa is affected. On the backs of the hands are numerous milia-like nodules and the scarring which is so characteristic of the disease. A tendency for the lesions to group is not present, and pruritus is not marked.

The Wassermann and Kahn reactions were negative. Histologic examination showed epidermolysis bullosa.

DISCUSSION

DR J FRANK FRASER I disagree with the diagnosis of epidermolysis bullosa on the basis of the microscopic findings. The histologic picture of epidermolysis bullosa is not specific, none of the bullous lesions are. There are some features, the position of the vesicle for example, which may lead one to favor one diagnosis or another, but these are not sufficiently characteristic to make a diagnosis on histologic grounds alone. The diagnosis in the present case must rest on the correlation of the histologic and clinical pictures. In my opinion this correlation is perfect, namely, microscopic vesicles and gross lesions which are typical of dermatitis herpetiformis.

DR JOSEPH J ELLER I agree with Dr Fraser regarding the diagnosis of dermatitis herpetiformis. I shall therefore not be surprised if this condition eventually develops into pemphigus.

DR GEORGE C ANDREWS (by invitation) I believe a drug eruption should be considered strongly, although I admit the likelihood of dermatitis herpetiformis.

DR GEORGE MILLER MACKEE I suppose the diagnosis of epidermolysis bullosa was based on two features: histologically, the subepidermic bulla or vesicle, and clinically, the traumatic lesions. In this particular instance, I do not think that these features combined are enough to warrant an unequivocal diagnosis of epidermolysis bullosa acquisita. The intense itching, generalization, grouping and long duration are in favor of Duhring's disease, and I think that in cases of severe, long-standing dermatitis herpetiformis one occasionally sees not only the traumatic feature but even in some instances a Nikolsky sign or pseudo Nikolsky sign and subepidermic vesicles on the hands. At present I am unwilling to rule out dermatitis herpetiformis.

DR HOWARD FOX Clinically, I think this case is a classic one of Duhring's disease. The so-called cardinal symptoms are present, including polymorphism, grouping, severe itching and a chronic course with tendency to relapse. This is apparently confirmed by Dr Fraser's opinion of the microscopic section.

DR FRANK C COMBES I agree with those who made the diagnosis of dermatitis herpetiformis reservedly. The patient is a fairly intelligent woman, and there are certain things in her history that are difficult to overlook. One has been already mentioned, the development of a bulla within fifteen minutes of trauma. Also, she awakes in the morning with bullae on her elbows from friction of the sheets when she turns over in bed during the night. I have never heard of that occurring in cases of dermatitis herpetiformis. I should like to know the cell count of the contents of the vesicles and whether eosinophilia is present. The potassium iodide test might be of some aid in differentiating between dermatitis herpetiformis and epidermolysis bullosa.

DR PAUL E BECHET I admit that the lesions resemble dermatitis herpetiformis. On the other hand, as was just pointed out, there is no doubt that trauma produces these lesions. They are most prominent on the ankles, legs and hands, places usually exposed to trauma. She presents numerous milia-like small nodules on the backs of her hands and large scars, both characteristic of epidermolysis. I am still of the opinion that the clinical evidence favors the diagnosis of epidermolysis rather than dermatitis herpetiformis.

Lupus Vulgaris of the Nose Multiple Pigmented Hemorrhagic Sarcoma
Presented by DR JOSEPH J ELLER

M C, an Italian aged 82, is presented from the New York City Hospital clinic for Dr Lloyd H Kest. The patient has had an eruption confined to the nose and adjacent areas for many years. The eruption has been persistent but has not spread and is erythematous and scaly and shows atrophy. Apple jelly nodules are seen on diascopic pressure.

On the lower portions of both legs and on both feet there are variously sized indurated nodules and plaques of brownish to purplish black. Edema has never been intense. The patient does not understand English, and it is most difficult to elicit a history.

The case is presented to show the presence of lupus vulgaris and Kaposi's sarcoma in the same person. The diagnoses were corroborated by microscopic study.

DISCUSSION

(The members agreed unanimously with the diagnosis as presented.)

Early Atypical Lupus Erythematosus Presented by DR PAUL E BECHET

H W, a Negro aged 27, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, states that his eruption has been present for six months. The patient had a penile chancre eight years previously and received continuous treatment for two years at the Social Hygiene Clinic of the Department of Health. The last injection was given a few days ago. The patient has typical syphilis, but on the right cheek are two erythematous, partially ringed lesions, with a raised but soft border. On the middle of the forehead at the hair line a similar lesion is present. The lesions are approximately 5 mm in diameter and are not scaly.

Histologic examination showed the early stage of lupus erythematosus.

Hypertrophic Lupus Erythematosus Presented by DR. PAUL E BECHET

F S, a man aged 49, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, was previously presented by Dr Max Scheer before the Manhattan Dermatological Society on Jan 9, 1940. He says his eruption has been present two and one-half years. The lesions consist of three oval areas, more or less confluent, situated on or about the lower lip and involving most of that area. They are dull red, with hard, raised, indurated,

rolled borders The central portions are atrophic and scaly The vermilion border is involved

Histologic examination confirmed the clinical diagnosis of lupus erythematosus

DISCUSSION ON DR BECHET'S CASES

DR J GARDNER HOPKINS The Negro is known to have syphilis, the lesions having a faint raised ridge at the border and a flattened scaly center I cannot see why those lesions could not be a cicinate syphilid or a fixed drug eruption There seem to be plenty of reasons why they are not lupus erythematosus There are no infiltration, adherent scales or telangiectases In the second case I also raise a question about that area with the soft, raised, red ridge at the border Of course, if it was proved histologically to be lupus erythematosus, one must discard the possibility of sarcoid, but clinically it looks more like sarcoid than like lupus erythematosus

DR EUGENE F TRAUB In view of what Dr Hopkins has said, I might say that one of the things in favor of the diagnosis of lupus erythematosus clinically in the case of the Negro is the fact that he has alopecia where the lesions are on the right cheek In addition to this loss of hair there are erythema and scaling It would be difficult to conceive of any disease other than lupus erythematosus that would cause loss of hair with erythema and scaling in that location

DR HOWARD FOX I agree with the diagnosis of Dr Bechet and the remarks of Dr Traub I do not agree that this lesion is an annular papular syphilid This manifestation of syphilis appears during the first six or eight months after infection and usually forms complete circles with hyperpigmented centers The infection in this case occurred eight years ago, and the patient has had continuous anti-syphilitic treatment

DR A BENSON CANNON I agree with Dr Hopkins The Negro's lesions on the forehead and right cheek are suggestive of erythema multiforme due to the arsphenamine that he has had or to phenolphthalein The lesion on the right cheek is only a macular blush, without infiltration, scaling, atrophy or telangiectasia Only the lesion on the right side of his forehead is a bit raised at the border, while the others are brownish blue, pigmented, macular and free of scaling I also agree that the lesion on the skin of the lower lip in the second case is more suggestive of sarcoid than of lupus erythematosus Again, the location is unusual for lupus erythematosus, and the oval, elevated, blue, shiny, red borders, with the center of the lesion hard and sievelike, are not symptoms that I would expect to find in a case of lupus erythematosus

DR HOWARD FOX In answer to Dr Cannon's suggestion that this condition might be a phenolphthalein eruption, it should be noted that this eruption has a raised border, which is not present in lesions due to phenolphthalein

DR PAUL E BECHET Both conditions are indicated histologically, but the clinical evidence is also in favor of the diagnosis of lupus erythematosus While the Negro has definitely had syphilis, he has had continuous antisyphilitic treatment for two years, the last treatment dating back only a few days ago The patches show a solid elevated plateau-like ringed lesion, entirely unlike the usual annular syphiloderm so frequently seen in Negroes The patches have been present for only six months Early lupus erythematosus is never scaly or hyperkeratotic Patulous follicular openings, so common in the chronic stage are also absent As in this case, the early stages of lupus erythematosus become manifest first as erythematous patches of a more or less fixed character, which later undergo edematous infiltration, with raised edges, and it is not until after several months or even years that it assumes the characteristic picture of the chronic discoid type

The second patient presents the hypertrophic mutilating type of lupus erythematosus, with lesions with greatly indurated, inflamed borders The condition is fortunately uncommon, as it is particularly resistant to treatment and on healing

leaves most unsightly scars I have observed cases in which it has eaten away a large section of tissue from the nose and after healing has left a deep punched-out scar

A Case for Diagnosis (Parapsoriasis? Purpura Annularis Telangiectodes?). Presented by DR PAUL E BECHET

T G, a man aged 48, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complaining of an eruption which has been present for seven or eight years In the summer it practically disappears but always recurs in the winter As it undergoes involution it leaves dark brown stains The lesions occur on the abdomen and flanks, as well as on the legs They are definitely telangiectatic and exhibit a tendency to annular formation

Two biopsies were performed, one of tissue from an early lesion on the left leg and the other of tissue from a much older lesion The histologic report suggested parapsoriasis and definitely ruled out purpura annularis telangiectodes (Majocchi's disease)

DISCUSSION

DR GEORGE MILLER MACKEE Dr Bechet said that purpura annularis telangiectodes had been definitely ruled out I presume this was because of the histologic architecture I examined the slide, though hastily, and it is true that I did not see any of the characteristic features of purpura annularis telangiectodes There was no panarteritis, no hyaline degeneration of the arterial walls and no sacculatation or herniation of the vessels These features are all absent, but this may be because only early lesions were examined In very early lesions there are edema of the blood vessels, perivascular infiltration, edema of collagen and hemorrhage These features are present in this case If another biopsy specimen is obtained, part of an old lesion should be selected I must admit, however, that typical changes usually occur in fairly young lesions In a typical case there are remissions and exacerbations, but the exacerbations may persist for three, six or even eight months or possibly a year Sooner or later, though, there is a remission, which may also last for months I understand that this patient is free from active lesions during the summer The large size of the lesions does not speak against purpura annularis telangiectodes There is such a thing as purpura simplex annularis, but usually it does not last for months I think there is at least a fair possibility that this case is one of aberrant purpura annularis telangiectodes Most patients have arthritic pain, but not all of them

DR EUGENE F TRAUB Dr MacKee said something about generalized lesions This patient has something rather indefinite on the left side of the trunk, but so far as I can tell, the eruption is limited to the lower extremities, from the hips downward

DR GEORGE MILLER MACKEE There are four lesions on the arms

DR EUGENE F TRAUB I do not think that dermatitis hemostatica is found on the upper extremities, but otherwise I do not see how one could exclude that diagnosis in a case of an eruption on the legs which comes and goes as this one does

DR HOWARD FOX My conception and that of the average dermatologist about purpura annularis telangiectodes is rather hazy I should like to ask Dr MacKee, who has made a special study of this disease, whether he knows of any case of eight years' duration in which the eruption has cleared up every summer

DR PAUL E BECHET There are lesions on the abdomen and the flanks as well as on the extremities This case is most interesting but difficult to discuss, in view of the histologic report by Dr Sachs that the microscopic examination was definitely against purpura annularis telangiectodes and in favor of parapsoriasis

Arsenical Keratoses Presented by DR A BENSON CANNON

L B, a girl aged 10 years, was presented before this society on Dec 19, 1939 (ARCH DERMAT & SYPH 41 962 [May] 1940), with a diagnosis of arsenical keratoses of the palms and soles

Examination showed a high amount of arsenic in the blood, 0.25 mg per hundred grams of dried blood. Her physician reports that he has established the fact that the thickening of the palms and soles appeared after treatment of her congenital syphilis with neoarsphenamine. He also states that the soles and palms cleared up after administration of arsphenamine was stopped, but the condition reappeared after resumption of the neoarsphenamine, and a generalized exfoliative dermatitis appeared. The child's palms and soles have improved rapidly under treatment directed toward the elimination of the arsenic.

Leukemia and Leukemid Presented by DR EUGENE F TRAUB

E D, a woman aged 64, was presented before this society on Dec 19, 1939 (ARCH DERMAT & SYPH 41 964 [May] 1940). At that meeting it was recommended that a biopsy be performed of one of the lesions on the fingers. Unfortunately, before I saw her again, she had received a $\frac{1}{4}$ skin unit dose of roentgen rays (75 r) on these lesions, and all of them had disappeared. When I saw her a few days ago, practically all of the cutaneous lesions, with one or two exceptions, were gone. Lately bullous lesions have been developing, which are quickly ruptured and become covered with a thick crust. None of these lesions have seemed suitable for biopsy, but should one develop that appears to be a leukemid, I shall try to obtain a biopsy specimen. The itching and other subjective symptoms are much improved.

BRONX DERMATOLOGICAL SOCIETY

MARION B SULZBERGER, M D, *President*

HENRY SILVER, M D, *Secretary*

Jan 25, 1940

Poikiloderma Vasculare Atrophicans (Jacobi) Presented by DR PAUL GROSS

J R, a man aged 39, has had a generalized eruption for the past three years, which began after an intensive exposure to sunlight. He has received various topical applications and injections but was never treated with roentgen rays. His general condition is good. He complains of dryness of the skin and a burning sensation in the cutaneous lesions.

The extensive eruption involves the trunk, arms and thighs and is made up of two types of lesions. The more recent lesions are yellowish pink, oval plaques, the size of half a dollar and covered with fine dry scales. The more advanced lesions are the size of a palm and larger, are dark red or cyanotic and consist of telangiectasia, mottled pigmentation and depigmentation. There are slight erythema and moderate scaling in these patches. The skin of the larger plaques shows wrinkling.

The Kahn and Kline reactions were negative. Urinalysis showed no abnormalities. Examination of the blood showed a normal value for hemoglobin and a normal cell count. Histologic examination of an early lesion showed normal epidermis, with slight hyperkeratosis in several places and a slight perivascular infiltration, with small round and occasional polymorphonuclear cells. Examination of an advanced lesion showed the epidermis to be of normal thickness, but the rete pegs were wiped out in several areas, and there was a definite invasion of the deeper layers by inflammatory cells. The corium showed a rather massive infiltration, with small round cells, few polymorphonuclear and eosinophilic leuko-

cytes and larger cells with pale nuclei. There were also some phagocytes containing brown pigment. In the subpapillary layer there was perivascular infiltration. The capillaries were somewhat increased in number but were of small caliber.

Poikilodermatomyositis Presented by DR PAUL GROSS

A B, a woman aged 30, born in Puerto Rico, was presented before the New York Academy of Medicine, Section of Dermatology and Syphilis, in November 1939 (ARCH DERMAT & SYPH 41:1187 [June] 1940)

Since that presentation there has developed on the right thumb an irregular yellowish area the size of a lentil and surrounded by a bluish zone of erythema. The yellowish infiltrate is firm and tender and suggests a deposit of calcium in the skin. There is also a contracture of the flexor tendons of the left palm.

DISCUSSION ON CASES OF DR GROSS

DR WILBERT SACHS The histologic structure in both cases is interesting. In the case of poikiloderma vasculare atrophicans the upper part of the cutis shows a rather dense cellular infiltrate, which is composed almost entirely of small round cells. The elastic tissue in the upper part of the cutis is either fragmented or absent. The absence of polymorphous cellular infiltrate, reticulum, mitotic figures and Pautrier abscesses rules out mycosis fungoides. The simple inflammatory process, the telangiectasia and the loss of the elastic tissue are characteristic of poikiloderma vasculare atrophicans.

In the case of poikilodermatomyositis the changes throughout the upper part of the cutis are similar to those in the first case. However, while the inflammatory process is somewhat less pronounced, the elastic tissue is entirely missing. In the lower portion of the section the muscle fibers are thin and closely packed. They are all arranged in rows, lying parallel with the epidermis. The elastic tissue in this area is fragmented. The changes in the upper portion are not unlike those found in poikiloderma vasculare atrophicans. In the deep portion, however, there are absorption and atrophy of muscle.

DR LOUIS CHARGIN Dr Sachs pointed out, as have certain other authors, that poikiloderma and dermatomyositis differ histologically as well as clinically. The case presented as one of poikiloderma is typical. The case of poikilodermatomyositis is questionable. It is true that now and then dermatomyositis in its later stages may present changes in the skin that are not clinically unlike that of poikiloderma, but certainly not early in the course of the disease. Neither in course nor in histologic picture are they identical, they are two entirely different diseases. Poikiloderma is an inflammatory disease, and dermatomyositis is a degenerative disease.

DR HENRY SILVER I also am of the opinion that little is gained by classifying the two diseases as one. I regard poikiloderma as a condition which is classified primarily with the cutaneous atrophies, and Dr Sachs just pointed out that until one finds changes in the elastic tissue one should not make the diagnosis of poikiloderma. Secondary involvement of various organs has been recorded by Petges and Cléjat, Jacobi and others. In other words, poikiloderma Jacobi is a condition which originates in the skin and is characterized by reticulated markings, thinning and wrinkling, pigmented spots, telangiectases, capillary hemorrhages, follicular brown-red pinpoint-sized and larger papules, red and bluish discolorations and whitish atrophic areas. Dermatomyositis, on the other hand, must be regarded as a systemic disease involving the skin, muscles and nervous system to a varying degree.

DR PAUL GROSS In the second case the diagnosis of poikilodermatomyositis is well established. The first case I consider of special diagnostic interest, because the histologic section of the advanced lesion of poikiloderma showed such massive infiltration that mycosis fungoides could well be considered. I was glad to hear from Dr Sachs that he is able to rule out mycosis fungoides on histologic grounds.

The main purpose of presenting these cases together was to show the distinction between poikiloderma Jacobi and poikilodermatomyositis. It is true that the cutaneous changes in dermatomyositis differ considerably from those in poikiloderma and that there exists a resemblance to lupus erythematosus of the acute variety. The scleroderma-like changes are the end product of the process in the skin, just as the sclerosis of the muscle is an end product of the myositis. Yet I do not agree with Dr Chargin that the condition is primarily a degenerative process. The inflammatory reaction of the skin and muscle during the earlier period of involvement is too pronounced, and the vascular damage in both tissues has been referred to recently by Guy, Grauer and Jacob (*ARCH DERMAT & SYPH* 40 867 [Dec] 1939).

Bismuth Line in the Long Bones of a Newborn Infant Presented by DR SAMUEL FELDMAN

This 1 month old infant is the child of Mrs M L, aged 30, who was presented before this society in October 1939 (*ARCH DERMAT & SYPH* 41 765 [April] 1940), with a lichen-planus-like eruption following the taking of arsphenamine.

The infant was apparently normal on physical examination. The Wassermann reaction of blood from the umbilical cord was negative. Roentgenograms of the bones revealed the presence of a heavy metal shadow (bismuth) manifested as a transverse line near the end of the diaphysis, particularly in both femoral and tibial bones and less marked in the ulnai and radial bones.

DISCUSSION

DR LOUIS CHARGIN According to Caffey (*Am J Dis Child* 53 56 [Jan] 1937), there is a definite relation between the time when bismuth is administered to the pregnant woman and the position of the bismuth line in the long bones, as judged by the roentgenogram. The position of the bismuth is directly related to the period of pregnancy, and the width of the line is determined by the amount of metal given. In the animal, Caffey has shown by experiment that the important anatomic change is the replacement of calcified cartilage matrix for the bone marrow spaces.

DR FRANK E CROSS In a prenatal syphilis clinic of the department of health routine roentgenologic studies of the long bones of infants were made about two weeks after birth. Some of the children had bismuth deposits in the epiphyses of the long bones.

DR SAMUEL FELDMAN The roentgenologist expressed the view that the line is comparable with any lead, arsenic or gold line, which is occasionally seen in the long bones of adults who have been given these metals. Since the mother did not come in contact with any of these metals, and since the administration of arsenic to the mother was discontinued after the second injection and treatment was continued with a bismuth compound only, it follows that this case is one of bismuth absorption and deposit in the bones. In the light of Dr Chargin's remarks about the time when the bismuth line appears, it would seem that the condition is in an early stage. There is also a definite deposit of new bone over the bismuth line.

Eczema Venenatum Due to Wooden Bracelet Presented by DR MARION B SULZBERGER

S T, a woman aged 52, was admitted to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec 31, 1938, with a sharply defined vesicular eruption on the left forearm above the wrist. Under routine local therapy the patient showed decided improvement during the second week of treatment and did not return to the clinic.

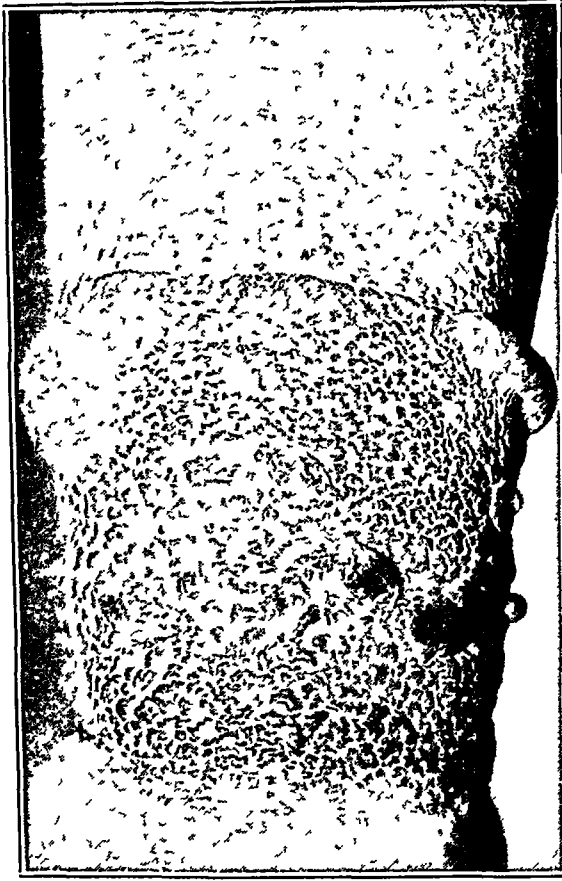


Fig 1—Four day old bullous reaction on the arm after the wearing of a wooden bracelet for only two hours

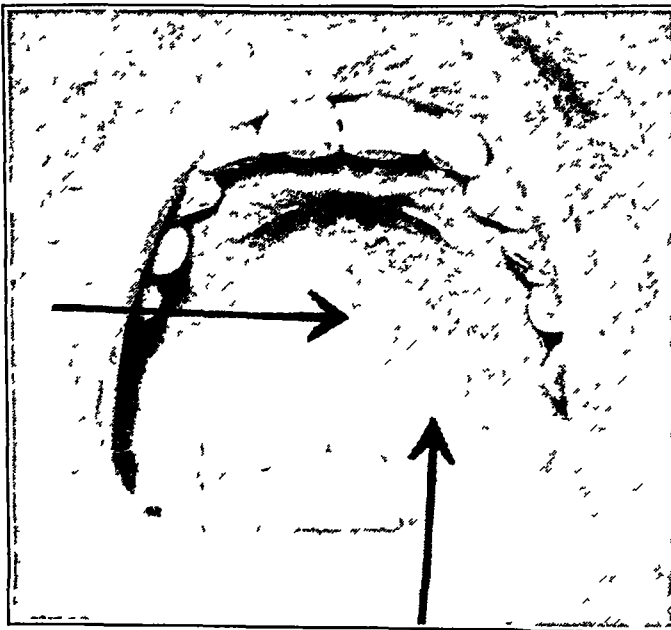


Fig 2—Reaction of mucous membrane of palate to scrapings of wooden bracelet

On Dec 19, 1939 the patient was readmitted, with a vesiculobullous erythematous eruption about 2 to 3 inches (5 to 7.5 cm) wide encircling the right forearm just above the wrist

Questioning disclosed that on December 16 the patient had worn a wooden bracelet for about three hours, which caused intense pruritus and some erythema. Several hours after the removal of the bracelet the eruption appeared. The same bracelet had been worn on the left forearm for several days about one year ago. The dermatitis last year was apparently due to the same cause.

On Dec 19, 1939 the mucous membrane of the left side of the hard palate was tested by applying scrapings from the wooden bracelet and holding these in place for five minutes. An erythematous papular lesion appeared at the site within forty-eight hours and disappeared within five days.

The family and personal history were not significant. There was no history of asthma, hay fever, urticaria or infantile eczema.

DISCUSSION

DR FRANK E. CROSS When Dr Sulzberger performs patch tests on this woman he will probably find that the dermatitis is due to the shellac or varnish covering the wood. I should like to mention the case of a young boy who presented a dermatitis under the chin. The chin rest of the violin was suspected. Patch tests with the varnish coating were performed, and a severe bullous reaction resulted in four hours. Judging from the severe dermatitis present in this case I should expect a similar reaction from the patch tests.

DR CHARLES LERNER I think that the eruption can be caused by the wood itself and not necessarily by the shellac. A short time ago I had a case of cheilitis in a musician, caused by French reed used in the mouthpiece of the musical instrument he played. The condition cleared entirely when Italian reed was substituted. Neither strip of wood had been covered with shellac.

DR MARION B. SULZBERGER I was unable to complete the tests to see what ingredients of the wood caused the dermatitis. The patient was presented because of the high degree of sensitivity and to show the severity of the local reaction as well as the associated sensitivity of the mucous membrane. As Dr Shelmire has recently shown, this association of mucosal sensitivity with cutaneous sensitivity in allergic eczema venenatum is more common than was previously supposed.

Eczema Venenatum from Nail Polish Presented by DR MARION B. SULZBERGER

R. C., a woman aged 37, was first seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov 14, 1939. The family history disclosed no cases of asthma, hay fever or cutaneous eruptions. The patient had been well until November 1938, when an itching eruption began on the eyelids and lips. The eruption gradually extended and eventually involved practically the whole face and neck, as well as the arms and chest. The patient received elsewhere a variety of treatments which consisted of roentgen rays, injections of sodium thiosulfate, estrogens, vitamins in high doses, ultraviolet and infra-red irradiation and fever therapy. The treatment was without effect. The eruption improved somewhat when she remained at home and did not use any cosmetics.

The patient presents redness and scaliness of both eyelids and a scaly, erythematous, scratched and somewhat thickened skin on the sides of the face and neck, on the chest and in the cubital spaces. The appearance of the eruption suggested a contact dermatitis, possibly due to some cosmetic. Patch tests performed with various cosmetics gave negative results. Attention was then called to the fact that nail polish and nail polish foundation had been omitted, and these were tested. The reaction to nail polish was 3 plus and to nail polish foundation 1 plus. On

closer questioning, it was then found that the onset of the dermatosis had occurred shortly after the first use of a new type of foundation for the polish.

With the use of soothing local treatment and the discontinuation of application of the nail polish and foundation, the patient improved rapidly and within a few days was entirely free of the eruption. She remained entirely well until patch tests with the offending preparations were performed, on December 26. Within twenty-four hours after this application, the previously affected areas showed a recurrence of the original dermatitis.

DISCUSSION

DR. MARION B. SULZBERGER: The patient is presented to call attention once more to this form of dermatitis. It occurs in women who are sensitive to one or more ingredients of the polishes used on their finger nails. The favorite sites are the eyelids and the face and not the hands or periungual areas. One has therefore to bear that in mind and to consider finger nail polish in investigating the eczematous eruptions of the eyelids so frequently seen in women.

Generalized Granuloma Annulare. Presented by DR. CHARLES PINES.

D. W., a school boy aged 9 years, was seen at the clinic of Bellevue Hospital on Nov. 23, 1939. The eruption began about eight months ago on the left leg and ankle. In the course of a few months numerous new lesions appeared on various parts of the body. The mother states that some of the lesions have undergone spontaneous involution, while others have remained stationary and have persisted to date. Physical examination gave essentially negative results except for showing enlarged tonsils and postnasal discharge.

On the chest, abdomen and buttocks and both upper and lower extremities there are raised, round or oval lesions with sharply elevated borders. The lesions are of firm consistency, either pinkish or skin colored, with a definite tendency toward grouping, and many have clear centers. There are no subjective symptoms. The tuberculin test with dilutions up to 1:10,000 gave negative results. Scrapings for fungi proved negative.

DISCUSSION

DR. WILBERT SACHS: I agree with the diagnosis of granuloma annulare, but I should like to have histologic confirmation if possible. This may not show granular degeneration. If so, it would be difficult to differentiate between the annular type of sarcoid and this type of granuloma annulare.

DR. H. VICTOR MENDELSON (by invitation): I saw this patient previously and hesitated to accept the diagnosis of granuloma annulare because of the multiplicity of the lesions and the limited number of typical lesions and because there was little or no tendency to spontaneous involution. However, the cases recorded in the literature, especially the one presented by Dr. Wise in which there were lesions on one hand and follicular lesions on the feet (ARCH. DERMAT. & SYPH. 40:291 [Aug.] 1939), bear great resemblance to the case presented. The histologic examination proved all the cases to be of granuloma annulare. I believe that this case is also one of granuloma annulare.

DR. DAVID BLOOM: Generalized eruptions of granuloma annulare are rare. I presented a little girl with such a condition (ARCH. DERMAT. & SYPH. 37:905 [May] 1938), who had less infiltrated lesions. While the lesions on the elbow do not suggest granuloma annulare, the diagnosis can be definitely made from the lesions on the body.

DR. HENRY SILVER: Is the generalized type of granuloma annulare more frequently observed in adults or in children? The few patients that I have seen were adults.

DR. CHARLES PINES: I believe that this condition is more frequently observed in children.

Chronic Discoid and Lichenoid Exudative Dermatoses Presented by DR MARION B SULZBERGER

A man aged 34, born in Poland, gives no family history of asthma, hay fever or cutaneous diseases. With the exception of undergoing an operation in 1932 for an inguinal hernia he was in good health until 1937, when the present eruption appeared on the thighs. The eruption cleared soon but recurred six months later. The patient was treated without success at Beth Moses Hospital, at the Essex Street Dispensary and at the King's County Hospital. In the last institution the eruption cleared in about six weeks but again recurred in two weeks, in August 1938. Ambulatory treatment until December was of little benefit. The patient was subsequently admitted to Montefiore Hospital for Chronic Diseases, where he remained until October 1939. The eruption cleared completely but relapsed within two weeks after he was discharged from the hospital. In December he was readmitted to the hospital.

The face, extremities and trunk present papular and discoid eruption. The lesions are round or oval and coalesce, forming bizarre shapes. There are numerous excoriations. The lymph glands are enlarged.

Examination of the blood showed 4,780,000 erythrocytes and 13,750 leukocytes per cubic millimeter, with 27 per cent eosinophils, 54 per cent neutrophils, 1 per cent basophils, 8 per cent small lymphocytes, 6 per cent large lymphocytes and 4 per cent lymphoblasts. Examination of bone marrow, according to the method of Arinkin, revealed an increase in eosinophilic polymorphonuclear leukocytes and the presence of eosinophilic myelocytes. A smear from the bone marrow showed 6 per cent myelocytes, 2 per cent myeloblasts, 2 per cent primitive cells, 10 per cent normoblasts, 11 per cent lymphocytes, 3 per cent monocytes, 48 per cent segmented polymorphonuclear leukocytes, 6 per cent staff cells and 12 per cent eosinophils. Histologic examination of an axillary lymph node showed subacute nonspecific lymphadenitis. The chemical examination of the blood showed 95 mg of sugar, 82 mg of urea, 150 mg of cholesterol, 98 mg calcium, 35 mg of phosphorus, 44 mg of albumin, 32 mg of globulin, 0.3 mg of bilirubin and approximately 0.02 mg of lead per hundred cubic centimeters and no arsenic. The Wassermann reaction with a cholesterol antigen was negative. The Kahn reaction was negative.

DISCUSSION

DR CHARLES A GREENHOUSE: Have any mental symptoms been observed in these patients, particularly during the periods of recurrence? It has been my experience that during an acute exacerbation there were definite symptoms of psychosis accompanied by moderate rise in temperature and superficial pustulation.

DR LEO SPIEGEL: I believe that all the patients whose cases were described by Sulzberger and Garbe were males. Have any cases been observed in which the condition occurred in females?

DR MARION B SULZBERGER: I have observed no definite example of this dermatosis in the female with the exception of a questionable one in a middle-aged woman. I have observed about 35 cases of this disease. I do not think there is anything noteworthy about the psyche of the patients excepting that itching, lack of sleep and other distressing effects of this chronic recurrent and incapacitating disease would cause the patient to act somewhat psychotic. However, other possibilities still exist, namely, that the nervous system may also be involved or may become involved as a result of the cutaneous disease.

DR EUGENE F KELLEY: Concerning the psychosis factor, I can report a case in which the patient was sensitive to turpentine and had repeated attacks of dermatitis from contact with it in his occupation. During the last attack he became comatose. All the symptoms cleared immediately after a spinal tap, the fluid was under pressure. The neuropsychiatrist was of the opinion that the meningeal irritation was probably due to sensitivity to turpentine.

DR. ADOLPH ROSTENBERG: I have observed a number of these cases. Of course, the patients suffered a great deal, but they were not neurotic. I do not think there is a neurogenic factor in these cases.

DR. MARION B. SULZBERGER: One sees a fairly typical picture in most cases, and the disease is easily diagnosed. It is about twelve years since I first began to observe these cases. I was first struck by the peculiarity of this dermatosis in Zurich and became more and more impressed by the fact that I could not fit it into any known group of dermatoses. It is important to stress that in none of my cases has the condition gone on to true lymphoblastoma (Sulzberger, M. B., and Garbe, W.: *ARCH. DERMAT. & SYPH.* 36:247 [Aug.] 1937). On the contrary, the patients with the older conditions have all become free of lesions, are well and are going about their work. If this disease were a forerunner of mycosis fungoides or lymphoblastoma, one would encounter more cases of lymphoblastoma, because the dermatosis is a relatively common condition. Then, too, the dermatosis is seen entirely in men, and lymphoblastoma has no sex predilection.

Serpiginous Syphilid and Nonsyphilitic Aortitis. Presented by DR. ARTHUR SAYER.

L. W., a laborer aged 63, born in Germany, has been living in the United States since 1893. He came to the clinic of Mount Sinai Hospital in December 1939, on account of vertigo, weakness and a cutaneous eruption of a few months' duration.

The patient presents a symmetric diffuse papular eruption on the upper and lower extremities. The lesions have the color of raw ham, are discrete and the size of a pea or grouped in serpiginous patches 2 to 3 inches (5 to 7.5 cm.) in diameter. There is moderate generalized adenopathy. The patient states that this cutaneous eruption has been present for the past five months. The Wassermann reaction was 4 plus.

He gave a vague history of a penile sore about forty years ago. He was never treated for syphilis. The blood was tested years ago, and the Wassermann reaction was found to be negative. He did not recall having had a recent penile lesion before the onset of the eruption.

The neurologic examination gave essentially negative results except that the left pupil was found to be slightly larger than the right. The urinalysis showed normal findings. The systolic blood pressure was 105 and the diastolic, 70. Electrocardiogram tracings showed the QRS complex to be blurred and the T wave in lead III inverted, changes indicating cardiac involvement. A roentgenogram of the chest showed no abnormalities in the lungs, the heart slightly enlarged and the aorta diffusely dilated and tortuous, most marked in the ascending portion and the upper part of the descending portion.

DISCUSSION

DR. LEO SPIEGEL: The lesions on the wrist impressed me as late serpiginous syphilid. I cannot offer a diagnosis for the lesions on the shoulder; clinically they are follicular papules. With regard to the aortitis, what evidence can Dr. Sayer furnish that it is not based on syphilis? Judging by the history which the patient gave, namely, that he had had a penile lesion forty years ago for which he was treated with "rubs," it appears that the aortitis is due to syphilis.

DR. LOUIS CHARGIN: The lesions on the hands especially suggest serpiginous papular syphiloderm and are likely a form of late secondary syphilis. The eruption is bilateral. Bilateral syphilitic eruptions are rare with late syphilis, but they do occur. Concerning the question of the nonsyphilitic character of the aortitis, I think the burden of proof is on the presenter. Certainly in a man of this age who had an infection many years ago and now presents a dilated aorta, the aortitis is more likely to be on a syphilitic basis.

DR. ARTHUR SAYER: There is no doubt in my mind that the man has a serpiginous syphilis and that the infection is rather recent. The history of a penile

lesion forty years ago is too vague to be accepted and certainly should not be considered as a primary lesion on that evidence alone. It could have been a herpes progenitalis or another type of nonsyphilitic lesion. The reason I believe the aortitis is nonsyphilitic is that his recognized syphilis is comparatively recent and could not cause this type of visceral lesion so early. Furthermore, the roentgenologist reports that the location of the aortitis and its tortuous character are against its being of syphilitic nature. It is also to be remembered that strenuous labor is occasionally responsible for aortitis—or, as Osler said, "Vulcan as well as Venus may cause aortitis."

Keratosis Follicularis (Darier) Presented by DR HARRY B FEILER

L G, a woman aged 21, was first seen about three months ago. She states that the lesions on the face, chest and thighs appeared about two years ago. No other member of the family is similarly affected. The father has psoriasis.

On the lateral aspect of the face, extending downward to the neck, the lateral and frontal part of the chest and merging at the lower half of the sternum there are grayish brown pigmented areas consisting of keratotic and verrucous lesions, varying in size from that of a pinhead to that of a lentil seed. Similar lesions, but at times so light that they are almost inconspicuous, are observed in the interscapular region and on the inner aspect of the thighs.

Histologic examination showed normal skin in the center of which there was a small lesion. It consisted of an area of hyperkeratosis and was apparently near a follicle or around a follicle. There was a characteristic horny plug containing some incompletely keratinized epithelial cells. There were also some partially degenerated epithelial cells which could be identified as corps ronds. The underlying epithelium showed some cellular irregularities and numerous mitotic figures, particularly in the remaining basal layer. A slight cellular infiltrate was present around the blood vessels in the cutis.

The histologic diagnosis was reported as dyskeratosis, consistent with the diagnosis of Darier's disease.

DISCUSSION

DR MARION B SULZBERGER. In spite of the fact that there are so few changes visible in this case, there already are two typical palmar "warts," which one sees so often in cases of Darier's disease.

DR HENRY SILVER. Conditions of this type are known as *formes frustes* of Darier's disease. It is important to stress that no other members of the family are affected. A few years ago I presented 4 members in one family who had the disease (ARCH DERMAT & SYPH 31 919 [June] 1935).

A Case for Diagnosis (Early Raynaud's Syndrome?) Presented by DR MAURICE UMANSKY

R R, a woman aged 23, noted three years ago that the right index finger became white when exposed to cold. She has never experienced any pain or swelling. Recently all her fingers and toes became similarly involved. Blanching occurred even in the summer during spells of chilly weather. Two sisters are afflicted in the same way.

When exposed to outdoor winter atmosphere the hands and feet become cold, clammy and bluish, with a diffuse cyanotic hue. The three middle fingers and toes are dead white, but their tips and the underlying parts of the nails are cyanotic. The radial pulse is the same on both sides. The skin presents no other abnormalities.

The patient gives a history of vague pains of the muscles of the back, shoulder, chest and feet since childhood. She is suffering from chronic left maxillary sinusitis with a postnasal drip and had until eight months ago frequent nosebleeds. Roentgen examination of the cervical portion of the spine showed the presence of spondylitis involving the bodies of the fourth, fifth and sixth vertebrae.

Examination of the blood showed 85 per cent hemoglobin and 8,500 leukocytes per cubic millimeter, with 54 per cent segmented polymorphonuclear leukocytes, 3 per cent staff cells, 39 per cent lymphocytes, 1 per cent eosinophils and 3 per cent monocytes. The sedimentation rate was four hours. The Kahn reaction was negative. The basal metabolic rate was —9 per cent. The urinalysis showed no abnormalities.

DISCUSSION

DR. DAVID BLOOM: This is an instructive case showing the difference between Raynaud's disease and sclerodactylia. With the former the skin is unchanged. Sclerodactylia may be associated with Raynaud's syndrome, for both are manifestations of a disturbance of the vegetative nervous system.

DR. MAURICE UMANSKY: The girl's condition is of a progressive nature. For two years only the right index finger was affected. Since the beginning of this winter all the fingers and toes have become involved. W. A. Pusey (ARCH. DERMAT. & SYPH. 19:467 [March] 1929) reported the case of a chauffeur who suffered from ischemia of one finger on exposure to cold. He considered the fact that the condition was limited to one finger as rare in the literature. In the light of the case presented the involvement of one finger seems to be an early stage of the condition which eventually spreads to the rest of the fingers. The condition in this case is apparently not due to endocrine disturbance. It is, rather, familial, since other members of the family suffer similarly. The early diagnosis of such a case of Raynaud's syndrome is important from the standpoint of therapy. Sympathectomy has to be considered. In the later stages of the syndrome, when bullae and gangrene set in (the other name of this condition is symmetric gangrene), the treatment is no longer effective.

Pigmentation of the Tongue Due to Bismuth. Presented by DR. CHARLES PINES.

C. C., a Negro fireman aged 38, has been under treatment at the Central Social Hygiene Clinic of the Department of Health for the past one and one-half years for neurosyphilis. On his visit to the clinic on Dec. 12, 1939 he complained of a sore on the tongue of a few days' duration. Examination revealed on the under surface of the right side of the tongue at the margin a tender and painful superficial ulceration covered with a grayish exudate. The tongue showed a grayish coating. The lesion was thought to be either traumatic or due to bismuth. A smear showed a few Vincent organisms. Several days later a bluish black pigmentation was noted on the under surface of the tongue at the site of the original lesion; this has persisted to date. The patch of pigmentation is surrounded by speckled areas of discoloration the size of pinpoints.

DISCUSSION

DR. DAVID BLOOM: I agree with the diagnosis of bismuth pigmentation of the tongue. It is a rare condition, although this case is the third that I have encountered in the past two months. In the other 2 cases which I have observed the pigmentation was located on the dorsum of the tongue. I have always thought that the pigmentation was due to a deposit of bismuth, but I have been recently advised by Dr. Satenstein that the pigmentation is due to melanin and not to bismuth.

DR. FRANK E. CROSS: Usually the pigmentation occurs on the under surface of the tongue. The usual bismuth line does not occur in this location.

DR. LEO SPIEGEL: This is an unusual case of bismuth discoloration in that the deposit is most pronounced in the area where the trauma occurred on the side of the tongue. The patient also has a severe bismuth stomatitis.

DR. CHARLES PINES: I believe that the reason for the development of the bismuth pigmentation on the tongue was largely the local injury sustained.

I recently observed a similar case at the Bellevue Clinic. A woman presented a bluish black line on the gums and discoloration at the tip of the tongue. The patient stated that she frequently pressed the tip of the tongue against the teeth. All who observed the case agreed that this habit, essentially trauma, was most likely the underlying factor in determining the location of the pigmentation.

Eczema Venenatum Due to Lipstick and Nail Polish Presented by DR HARRY B FEILER

I V, a girl aged 17, was first seen at the clinic of the Lebanon Hospital in August 1939. She states that in the latter part of June an eruption appeared on the face. When seen in August the patient presented an erythematous, scaly eruption around the right eye, in an area of adjacent skin extending laterally to the hair margin and oblong patches on the right side of the neck. Under soothing local applications the eruption disappeared. One month later there developed a dermatitis involving the lips. An eruption similar to the previous one recurred and again involved the face, neck and ears.

Patch tests with petrolatum, yellow wax, cetyl alcohol, paraffin, stearic acid (a combination of stearic acid and castor oil), tetrabromofluorescein, brilliant red, royal scarlet, maroon Almay, 0.5 per cent eosin in 80 per cent alcohol, nickel, silver, rouge, oil of bergamot, Marvelous mascara, powder and rouge, mirror-glo nail polish and Beverly nail polish gave negative reactions. Patch tests with Almay perfume, Style-set lipstick and Platinum nail polish gave positive reactions.

DISCUSSION

DR MARION B SULZBERGER. It is possible that this patient is sensitive to some essential oil which is present in all three articles to which she gave positive reactions.

In regard to so-called nonallergic cosmetics, they are nonallergic in that there are several important allergens eliminated (orris root and oil of bergamot), but they still contain perfume, dyes, certain essential oils and various other ingredients. A sensitized patient may therefore react to a "nonallergic" cosmetic as well as to any other brand.

PHILADELPHIA DERMATOLOGICAL SOCIETY

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Feb 23, 1940

A Flesh-Colored Paste to Camouflage Cutaneous Lesions Presented by DR JOSEPH V KLAUDER and DR ELMER R GROSS, Wilmington, Del

Two patients with lupus erythematosus are presented to demonstrate that a paste has made their lesions considerably less apparent, with consequent improvement in appearance, making it possible for 1 of the patients to resume work. The formula of the paste, modified from that of E Daubresse-Morelle (*Rev franç de dermat et de vénéréol* 14 355, 1938), is as follows:

Glycerin	16.8 parts	Titanium oxide	40.0 parts
Distilled water	19.8 parts	Zinc oxide	17.0 parts
Egg albumin	1.0 part	Iron oxide	5.0 parts
Purified siliceous earth	0.1 part	Liquid petrolatum	0.5 part

(Powdered ochre [q s] may be added to make a darker shade.)

One patient prefers this application to the proprietary "covermark," since the latter dried and cracked on the skin. Theatrical grease paint was tried but was

discontinued, since it was greasy, rubbed off, did not absorb perspiration and was difficult to remove. None of these objections apply to the paste now being used.

DISCUSSION

DR. FRED D. WEIDMAN: Is there any difference in the satisfactoriness of the application in summer and in winter?

DR. JOSEPH V. KLAUDER: One can easily add a preservative to eliminate the possibility of bacterial action in summer.

DR. FRED D. WEIDMAN: In the laboratory my associates and I use a mounting solution—Farrant's solution—which contains egg albumin, and in order to prevent decomposition we add arsenic. For other watery solutions we use thymol. Arsenic would not be altogether satisfactory as an ingredient of a face cream, but thymol might be satisfactory. In a mixture containing albumin it is necessary to inhibit the growth of micro-organisms.

DR. JOSEPH V. KLAUDER: The odor of thymol might be objectionable in a face cream.

Nonspecific Effect of Antisyphilitic Treatment in Inflammatory Ocular Lesions (Chorioretinitis). Presented by DR. JOSEPH V. KLAUDER.

I. C., a white woman aged 32, was first seen on June 8, 1939, with central chorioretinitis of both eyes. Her complaint was poor vision, which had first appeared three years previously. She had been hospitalized and studied by various ophthalmologists and ineffectually treated by many procedures, including intravenous injections of typhoid vaccines and injections of old tuberculin and streptococcus vaccine. No evidence of a focus of infection could be discovered. Repeated examination of the blood yielded negative Wassermann reactions, and examination of the spinal fluid also gave negative results. Physical examination for syphilis gave negative results, and the family history did not reveal any syphilis. The patient had never been pregnant. Ophthalmoscopic examination of the right eye disclosed opacities of the vitreous; the disk was oyster gray; the margins were blurred, and the macular region was inflamed, with areas of exudative retinal atrophy pigmentation. A clear view of the fundus of the left eye could not be obtained, on account of opacities in the vitreous; the disk was pale, and areas of pigmentation could be seen around the disk. Vision was 1/45 in the right eye and 6/22 in the left. Although the diagnosis of syphilis could not be established, antisyphilitic treatment was administered on June 17. This consisted of 30 grains (1.94 Gm.) of potassium iodide orally three times a day, two injections of an oil-soluble bismuth compound at weekly intervals and neoarsphenamine weekly, beginning with 0.1 Gm. and increasing to 0.3 Gm. Soon after treatment was instituted an appreciable improvement was apparent. The vitreous opacities became less, and the retinal choroidal inflammation began to subside. On June 29 the vision in the right eye was 2/45 and in the left was 6/12. The improvement was progressive, so that in September 1939 examination of the right eye disclosed considerably less opacity in the vitreous; the disk was somewhat whitish; the margins were much less blurred; there was some retinal atrophy about the disk, and in the macular area there was fine, disklike choroidal pigment. The left eye showed less opacity in the vitreous; the disk was blurred, with some swelling of the nasal portion, and about and below the disk there were patches of retinochoroiditis, a blotch of pigmentation and areas of retinal atrophy. In December 1939 binocular vision was 6/9.

Nonspecific Effect of Antisyphilitic Treatment of Patients with Inflammatory Ocular Lesions (Chorioretinitis). Presented by DR. JOSEPH V. KLAUDER.

P. M., a white woman aged 24, was referred to me in September 1939 for testing the nonspecific effect of antisyphilitic treatment of chorioretinitis of the

right eye of four months' duration. Extraction of two teeth, tonsillectomy and treatment directed at a possible sinus infection had no effect on the ocular condition. There was no other clue as to the cause of the chorioretinitis. Repeated Wassermann tests gave negative reactions. The patient is married and has a healthy child aged 3 years. She has had no miscarriages or stillbirths. Her husband stated that he has never had a venereal disease. Physical examination gave essentially negative results. Ophthalmoscopic examination of the right eye showed opacities in the vitreous, and the disk was oval and slightly blurred. Extending from the disk to the temporal side of the retina there were large areas of recent and old chorioretinitis. The vision of the right eye was 4/6. The left eye was uninvolved and had normal vision. Weekly injections of an oil-soluble bismuth compound were started on September 30. These were followed by a course of weekly injections of 0.45 Gm of neoarsphenamine. Potassium iodide was given orally. Soon after this treatment there was appreciable subsidence of the inflammation. The improvement continued. Two months later there were no active inflammatory areas, and the chorioretinitis had retrogressed.

DISCUSSION OF DR KLAUDER'S CASES

DR JOSEPH V KLAUDER: These cases raise the question as to whether the patient had syphilis, since the regression of the lesions under antisyphilitic treatment was like the response of syphilitic lesions. There was an appreciable improvement, with lessening of the inflammatory reaction, after one injection. However, there was no clinical evidence to support the diagnosis of syphilitic chorioretinitis. I thought it would be worth while to determine the nonspecific effect of syphilitic treatment in patients with inflammatory ocular lesions. The frequent use of mercury by the ophthalmologist apparently exerts a nonspecific effect. I do not know of any series of cases in which the effect of a bismuth compound or neoarsphenamine rather than of mercury was studied. Gold sodium thiosulfate has been used in the treatment of lesions suspected of being tuberculous, but the ophthalmologists are not yet making use of arsenic and a bismuth compound for the nonspecific effect which I believe the substances exert on certain inflammatory ocular lesions.

Old Blood Vessel Remains of Interstitial Keratitis Presented by DR JOSEPH V KLAUDER

L. C., a white girl aged 16, had active interstitial keratitis in the right eye in 1934, for which she received sixty-seven injections of bismuth subsalicylate and twenty-five injections of neoarsphenamine. The Wassermann reaction of the blood is now negative. There are no stigmas of congenital syphilis. The corneas are clear on gross inspection. However, there are old blood vessels in the right cornea which are diagnostic of interstitial keratitis. These can be demonstrated by slit lamp examination and with the plus 20 lens of an ophthalmoscope.

DISCUSSION

DR JOSEPH V KLAUDER: This patient illustrates the importance of the slit lamp in the clinical diagnosis of congenital syphilis. Aside from the history of "sore eyes" and the slit lamp findings, she has no evidence by which the diagnosis of congenital syphilis (interstitial keratitis) could be made.

DR DONALD M PILLSBURY: When do you think a patient with interstitial keratitis should be treated with nonspecific therapy? What are the criteria for changing from standard treatment to some form of fever therapy?

DR JOSEPH V KLAUDER: I think it desirable to use fever therapy routinely, if only in the form of vaccine in conjunction with standard therapy. My routine is to give a vaccine intravenously every other day in conjunction with antisyphilitic therapy. Malarial therapy is employed in selected cases. If nonspecific therapy is not used routinely, I should select patients in whom the interstitial keratitis is severe or is not progressing favorably.

DR. ALFRED COWAN (by invitation): The slit lamp picture sometimes seen in patients with syphilitic interstitial keratitis is classic. One usually sees a density in the posterior portions of the cornea (a sort of thin, translucent loss of opacity), while the anterior portion of the cornea is clear. The blood vessels may be so small and thin that they may be mistaken for anything but blood vessels. In nearly every case massage of the eye stimulates the circulation sufficiently to make it certain that the structure seen is a blood vessel. In my experience these vessels are permanent, in spite of repeated statements to the contrary. They appear in a peculiar fashion. First one sees endothelial strands, which gradually enlarge to fair-sized vessels. When the acute process subsides, they contain no blood unless they are stimulated by massage. In some cases the interstitial keratitis heals so well that one cannot tell by superficial examination whether the eyes were ever affected. One should never, however, give a prognosis with regard to the end result of interstitial keratitis. I have observed some cases in which the condition was so severe that the corneas were almost as opaque as a piece of paper and yet at the end of about a year the patient had almost normal vision. On the other hand, I have seen apparently mild involvement result in such scarring that the vision becomes seriously affected. I think interstitial keratitis would disappear if one did not give antisyphilitic treatment at all.

Blood Vessels in Cornea Thirty-Five Years After Interstitial Keratitis.

Presented by DR. JOSEPH V. KLAUDER.

K. W., a white woman aged 45, when 10 years of age had interstitial keratitis. Treatment consisted only of mercury rubs. She has been married for sixteen years. Her 2 children, aged 15 and 12 years, are in good health, presenting no evidence of syphilis of the third generation. On examination the patient has a suggestive facies of congenital syphilis. Her upper teeth have been removed. There is a small, faint opacity in each cornea. Old blood vessels of interstitial keratitis were seen with the plus 20 lens of the ophthalmoscope, and slit lamp examination of the cornea revealed changes characteristic of old interstitial keratitis (J. A. M. A. **113**:1624 [Oct. 28] 1939). The vision in the right eye was 6/30, and with correction, 6/15 plus 1. In the left eye it was 6/21, and with correction, 6/9. The Wassermann reaction of the blood was doubtful.

DISCUSSION

DR. JOSEPH V. KLAUDER: Carvill and Derby (*Boston M. & S. J.* **193**:403, 1925) published a comprehensive study of interstitial keratitis, in which they compared the final vision of treated patients with that of a similar number of untreated patients. In the treated patients the final vision was better.

Interstitial Keratitis at the Age of Sixty. Presented by DR. ELMER R. GROSS, Wilmington, Del.

F. L., a white man aged 60, had bilateral interstitial keratitis at the age of 25, for which he received only local treatment. One young brother had interstitial keratitis. The patient had no recurrence until November 1939, when the right eye became actively involved. Examination reveals that he is edentulous and has a congenital syphilitic facies. He has eighth nerve deafness. The vision in the right eye is 1/60; in the left eye it is 2/60. Slit lamp examination of the right eye showed extensive scarring of all the layers of the cornea, more pronounced in the pupillary and nasal half. There was definite increased relucency of the posterior surface and moderate pigmentation of the scars, especially at the lower third. There was moderate deep vascularization. The anterior chamber was deep. There was slight atrophy of the iris stroma. The lens appeared hazy by reason of the corneal opacities. The left eye showed the same changes as the right eye except that scarring was less extensive. There was definite increase in relucency of the posterior surface, with several deep vessels seen. The lens appeared to be clear,

with increased relucency of the suture lines. The slit lamp diagnosis was old interstitial keratitis of both eyes. The Wassermann reaction of the blood was strongly positive.

DISCUSSION

DR JOSEPH V KLAUDER: I think the oldest patient with interstitial keratitis reported in the literature was 70, the youngest was 2 years.

DR ROBERT KIERLAND (by invitation), Rochester, Minn.: I do not believe that at the Mayo Clinic progress is made beyond what is done here in the management of interstitial keratitis. Nonspecific therapy is used at the clinic, particularly malaria.

DR JOSEPH V KLAUDER: How young are the patients you treat with malaria?

DR ROBERT KIERLAND (by invitation), Rochester, Minn.: The youngest I have seen treated with malaria was 12 years. That treatment is given to any patient over 4 years of age, provided the general condition is good, with careful watching for reactions.

Atrophy of the Optic Nerve. Old Interstitial Keratitis (Malaria Therapy)

Presented by DR MARJORY HARDY (by invitation), Norristown, Pa.

E. B., a white woman aged 21, had "sore eyes" six years ago, for which she received only local treatment. She now complains of almost continuous headaches. Examination reveals a definite congenital syphilitic facies, a high palatal arch, poor dental hygiene, a suggestion of bowing of the right tibia and exaggerated reflexes. Examination of the fundus revealed a pale right disk, with sharply defined edges. The vessels were macular, the periphery was normal. The entire fundus was distorted. The left eye was the same as the right except that pallor of the disk was less evident and was more confined to the temporal side. The pupils were equal and fixed to light. A corneal haze was seen grossly. On Feb. 8, 1939 the vision was 6/60 in the right eye and 6/30 in the left eye. The slit lamp examination revealed old interstitial keratitis of both eyes. Starting on November 13 the patient was given malarial treatments. She had nine major crises. This was followed by the administration of bismuth compound and of neoarsphenamine. The serologic reactions on November 3 were Wassermann, positive, and Meinicke, weakly positive. On November 10 the examination of the spinal fluid showed reaction for globulin, weakly positive, colloidal gold curve, 0000000000, and Meinicke reaction, negative. On November 30 the spinal fluid showed reaction for globulin, negative, colloidal gold curve, 0000000000, and Kolmer reaction, moderately positive.

DISCUSSION

DR JOSEPH V KLAUDER: This is the first combination of atrophy of the optic nerve and interstitial keratitis I have seen in this clinic. I have seen patients with interstitial keratitis who have had pupillary abnormalities with normal spinal fluids. The association of active neurosyphilis with interstitial keratitis is not common.

Pemphigus of the Mucous Membranes, Ocular Pemphigus (Remissive Stage)

Presented by DR JOSEPH V KLAUDER

M. G., a white woman aged 57, who was presented at previous meetings of this society (*ARCH. DERMAT. & SYPH.* 27:718 [April] 1933, 37:364 [Feb], 687 [April] 1938), has been under observation since 1931. She also has argyria and lupus erythematosus of the scalp. During the active stage of the condition lesions were noted in the various mucosal surfaces. A vesicle was seen on the conjunctiva along with acute conjunctivitis, vesicles and erosive areas were present in the mouth, erosive areas occurred on the nasal septum, in the vagina and on the anal mucosa. The oral lesions first appeared in 1920, and the ocular involvement began in 1929. Treatment with injections of gold sodium thiosulfate

and a bismuth compound for the lupus erythematosus seems to have influenced the pemphigus favorably, since it has remained quiescent for a longer period than any time since its appearance. There have been no oral vesicles since about September 1938, and there are only occasionally a few erosive areas. The ocular involvement is now quiescent. The cul-de-sacs are narrowed. The conjunctiva is thickened and wrinkled, and there is an external symblepharon in the right eye. The corneas are uninvolved, and therefore her vision is good. The underlying pathologic process, which causes shriveling of all mucous surfaces, is fortunately concentrated in the mouth and vagina and not in the eye. The vagina is almost obliterated. The patient is shown especially to demonstrate areas of scarring on the buccal mucosa. There is a linear, cordlike scar on the right side. There is a rounded scarred area on the left side of the nasal septum.

DISCUSSION

DR. HOWARD EARLE TWINING: Has this patient ever shown any cutaneous lesions?

DR. JOSEPH V. KLAUDER: No, I observed vesicles only on mucous surfaces. Your patient with ocular pemphigus who was to be presented at this meeting was the only patient I had seen with ocular pemphigus and also bullous lesions on the skin. After reviewing the literature and after studying a number of patients with the disease, I have changed my opinion and now believe that ocular pemphigus is a part of pemphigus of the mucous membranes and is in some way related to pemphigus of the skin.

DR. DONALD M. PILLSBURY: I should like to suggest that in any cases of argyria recorded in the future an attempt be made to determine as exactly as possible how much and in what concentration the silver salt was used. I think these data should be obtained, in view of the new requirements of the Food and Drug Administration.

DR. ABRAHAM STRAUSS: Why does one rarely see ocular lesions in cases of true pemphigus? Is it because they are distinctive conditions or different clinical aspects of the same condition?

DR. JOSEPH V. KLAUDER: I do not know. There are cases of ocular pemphigus reported in which pemphigus vulgaris subsequently developed with death as the result. The concept of ocular pemphigus embraces the appearance of vesicles on the conjunctiva and usually other mucous surfaces, a subconjunctival inflammation which leads to contraction, shriveling of the conjunctiva and its obliteration. The disease is progressive and is often confused with trachoma. Duke Elder stated that if the patient lives long enough blindness will eventually ensue.

Interstitial Keratitis (Malaria Therapy). Presented by DR. JOSEPH V. KLAUDER.

N. B., a white girl aged 19, when first seen, in November 1939, had active interstitial keratitis of the left eye of one month's duration. The right eye was uninvolved. The left cornea was diffusely hazy. Vision was: left eye, counting fingers at 6 inches (15 cm.), and right eye, 6/6. Slit lamp examination of the left cornea confirmed the clinical diagnosis of interstitial keratitis. The patient had nine attacks of fever, with temperatures ranging from 103 F. to 105 F., beginning on November 16. Prior to malarial inoculation, she received three injections of a water-soluble bismuth compound and three injections of neoarsphenamine. During malaria therapy there was a prompt subsidence of subjective symptoms, and the cornea became less hazy. Administration of the bismuth compound and neoarsphenamine were resumed after the malarial treatments were stopped. Vision in the left eye is now 6/15 plus 1; there is no inflammation, and the cornea shows a faint opacity in the center. The right eye became involved about February 15.

DISCUSSION

DR JOSEPH V KLAUDER It is of interest to note that, although the first eye did well after malarial therapy, the involvement of the second eye was not prevented. An analysis of records of patients receiving different forms of treatment now being conducted although not yet completed shows so far that best results are obtained from fever therapy, in addition to administration of arsenic and bismuth compounds.

A Case for Diagnosis (Dermatitis Herpetiformis? "Id"?) Presented by DR LEWIS M JOHNSON (by invitation) for DR CARROL S WRIGHT

B R, a white man aged 30, with a history of susceptibility to "sun poisoning" and of having received treatment for "allergic rhinitis," when first seen, on Sept 29, 1939, presented the typical picture of tinea of the soles and eczematization of the penis and scrotum. The rest of the eruption was suggestive of a dermatophytid. He now presents a generalized dermatitis that occurs in patches, some of which are flat and scaly and others thickened with eczematization and a tendency to crust. These patches tend to coalesce in some areas. He also exhibits considerable excoriation, but the scratch marks are not the predominant factor, since he also shows secondary changes due to superimposed infection. The eruption began in August 1939, as a pruritic vesicular penile eruption. It spread to the groin as a patchy, weeping and crusting papulovesicular dermatitis. Two weeks later it occurred on the hands and feet, and in another week it was on his face and back. This eruption improved somewhat during the occasions when the patient was hospitalized but promptly recurred when he went home, and at present the eruption is practically generalized and extremely pruritic. The patient is well nourished, intelligent and apparently free from any nervous instability. No foci of infection have been detected, but he has a more or less pronounced lymphadenitis. His physical status is normal. The urine is normal. Blood counts on two occasions showed some reduction in hemoglobin, with a normal erythrocyte count. The lymphocytes were somewhat increased, and there were 32 and 21 per cent eosinophils. A serologic test for syphilis gave a negative result. The patient has been given various local applications, chiefly antipruritic and antiseptic, which gave only temporary benefit. He has also had, parenterally, calcium gluconate, vaccines, whole milk and liver extract. Internally he has had alkalinizing medication, massive doses of vitamin D, iodides and sedatives. Mild roentgen ray therapy has improved certain areas only. Histologic study of the skin revealed a possible hematogenous process, such as may occur with rheumatic dermatoses. The picture was inconsistent with that of atopic dermatitis, particularly since the changes occurred so deeply in the tissue. The changes in the lymph node were inflammatory, but the possibility of a lymphoblastomatous process could not be excluded, especially Hodgkin's disease, in view of the eosinophilia.

DISCUSSION

DR FRED D WEIDMAN I have studied the sections from this case. There is at least one milium abscess deep in the corium, which is hard to reconcile with any of the clinical features seen tonight, and after seeing the dermatosis, I shall have to consider the abscess as being possibly the result of secondary infection. I did find at one place, where there was the least scratching (the posterior axillary fold), a certain annular arrangement of some of the papules. I suggest that this condition may be a beginning dermatitis herpetiformis and recommend the iodide test. The lesions are entirely too sharply circumscribed and discrete for the eruption to be an expression of an atopic dermatitis.

DR ABRAM STRAUSS This case is somewhat similar, I believe, to one I presented two meetings ago. The patient was a young Negro from the Eastern Penitentiary, and I believe the consensus then was that he had more or less an "id" eruption.

DR. LEWIS M. JOHNSON (by invitation): I considered the possibility of dermatitis herpetiformis. My first impression was that this condition was an "id," and the lesions on the feet and hands particularly looked as if they might be of fungous origin. However, since then the eruption on the feet and hands has cleared up.

Telangiectatic Dysplasia of the Rendu-Osler-Weber Type, with Pigmentary Changes. Presented by DR. JOSEPH V. KLAUDER.

Mrs. D. T., a white woman aged 50, has had "red spots" on her skin as long as she can remember. Her sister has similar but smaller numbers of "red spots" on her skin, and her mother had the same. The patient does not know whether her sister and mother ever had nosebleed or other hemorrhages. She is subject to nosebleed, having usually two severe attacks each year. The gums bleed easily when she uses a toothbrush. There is no history of other hemorrhages. About twenty years ago a large area of pigmentation appeared on the inner surface of the right arm and subsequently disappeared. Five years ago pigmentation appeared and has since persisted in the axillas, on the upper inner surface of the thighs and on the lower aspects of the legs. She perspires freely; her face flushes readily; she has frequent attacks of palpitation, and she sneezes eight to ten times consecutively some mornings. Her blood pressure is 180 systolic and 85 diastolic. On the flush areas of the face and on the nose there are telangiectatic vessels, with a few red puncta. The lips and buccal mucosa are normal. The tongue is of the scrotal type but is otherwise normal. There are telangiectases on the soft palate and on the uvula. The conjunctivas are normal, and the fundi show no abnormalities of the vessels. On the nasal septum there is a bright red punctum covered with a hemorrhagic crust and with radiating telangiectases. On both surfaces of the upper extremities and on the trunk there are scattered "ruby spots" (De Morgan spots), so-called angiomas. These are bright red, discrete and slightly elevated. On the upper extremities there are a great number of bright red puncta. Pressure around the arms with the cuff of the sphygmomanometer does not increase the number of puncta. On the inner surface of the right arm there are light brown puncta and telangiectasia-like lesions; some are crescentic, and there are two ill defined circinate lesions. Here the appearance is suggestive of angioma serpiginosum. In both axillas and on the upper surfaces of the arms there are discrete spots and irregularly shaped patches of pigmentation, varying from light to dark brown to black. The upper inner surface of both thighs is similarly involved. The pigmentation is more pronounced here, and in the center of some of the pigmented patches there is a bright red spot. On the cubital spaces and on the flexor surfaces of both wrists there are linear and rounded areas of light brown pigmentation. The hands are uninvolved. On the upper part of the chest there are scattered areas of telangiectasia. On the legs and thighs there are scattered bluish arborescent telangiectases of the type commonly seen in women. On the lower third of both legs there are large dilated venules and irregularly shaped areas of reddish brown pigmentation, on the borders of some of which there are pinpoint-sized reddish puncta and telangiectasia-like reddish brown lesions. Here the appearance is suggestive of Schamberg's disease.

DISCUSSION

DR. FRED D. WEIDMAN: William Egbert Robertson (*Ann. M. Hist.* 6:255 [May] 1934) stated the belief that he had observed the bright lesions appearing during attacks of acute cardiac decompensation. Their location in dependent positions around the ankles and legs of this patient suggests the desirability of studying her circulatory system. The fact that they have been present as long as the patient can remember would tend to discredit the idea that they are the kind of telangiectases about which Dr. Robertson has written. I suppose that the combination of the hereditary vascular weakness with possible cardiac decompensation at this woman's age could explain the localization of the lesions to the dependent position, where factors of stress and strain are in operation.

DR DONALD M PILLSBURY One cannot yet be entirely certain that the pigmentary changes are associated with hemorrhage. In the first place, this woman has a definite stasis, and it seems to me that the lesions on the ankles are compatible with the result of a stasis pigmentation. The axillary lesions did not show definite telangiectases, but the woman is certain that these come and go. They first appeared about twenty-one years ago. The lesions always appear during the summer months, a time when one would expect an intertriginous effect in the axillas. I think a little more proving will have to be done before this case can be accepted as one of Rendu-Osler-Weber syndrome associated with pigmentation.

DR FRED D WEIDMAN I assumed that it had been proved that the condition was Osler's syndrome, in view of the history of epistaxis.

DR JOSEPH V KLAUDER Dr Weidman's remarks concerning Robertson's explanation of these angiomas is one view. Another view, that of Weber, is that the angiomas are evidence of a telangiectatic dysplasia. That view would exclude capillary weakness as a cause. It is true that the pigmentary changes might not be part of that condition, but I believe they are. The patient obviously has a pathologic process involving the capillaries. The picture she presents is not a typical Osler's syndrome. Telangiectases in the Osler syndrome are most common on the hands, lips and tongue, but this patient has none at these sites. She does not have any of the spider type of telangiectases, which are also frequently seen with Osler's disease. On the thigh she has pronounced pigmentary patches, and in the centers of some of them are definite angiomatous red puncta. I think it is reasonable to associate the pigmentation with the capillary condition. I believe this patient's condition belongs in the group of diseases reported by Weber as telangiectatic dysplasia of the Rendu-Osler type (*Brit J Dermat* 51 468, 1939).

NOTE.—The patient states that she did not use cologne water or any cosmetic in the axillas or on the upper inner surfaces of the thighs. Her sister has a number of angiomas and red puncta scattered over the surfaces of the arms and legs, with fewer on the skin of the trunk, she is not subject to nosebleed.

A Case for Diagnosis (Keratosis Palmaris et Plantaris, Acquired Type, or Haxthausen's Disease?) Presented by DR HOWARD EARLE TWINING

A R, a white woman aged 44, about a year ago began to notice a progressive thickening of the palms and soles. She does not complain of itching or burning but does have pain due to cracks and fissures. There is no hyperhidrosis. The hands show a decided thickening of the epidermis, which not only involves the palms but extends onto the extensor surfaces of the fingers and the backs of the hands as well. The nails are only slightly involved. The extensor surfaces of both forearms to the elbows are also somewhat thickened and scaly. The soles are symmetrically hyperkeratotic, in some areas about 0.75 cm in diameter, especially over pressure areas. The ankles are comparatively free. An erythematous contiguous border extends over the heel and lateral aspects of the feet. Some of the toe nails are thickened. The interdigital webs are comparatively free. The Wassermann and Kahn reactions of the blood were negative. There were no fungi in scrapings. The patient has been given estrone, 1 cc intramuscularly twice weekly, and 10 per cent salicylic acid ointment, with decided improvement after three weeks.

DISCUSSION

DR FRED D WEIDMAN This woman has had rheumatism for several years. The combination of these keratotic lesions makes one think of gonococcal infection. Has this possibility been investigated? I do not recall having seen gonorrheal keratosis in a female.

DR HOWARD EARLE TWINING This patient was studied in the gynecologic and orthopedic departments before she was referred to me, but so far as I know there was no test made for gonorrhea. The history of keratosis coming on about

three years ago after complete hysterectomy suggested that the patient may have keratoderma climactericum, and for that reason she was treated with estrone for three weeks. Under this therapy the lesions have cleared up anywhere from 25 to 30 per cent.

A Case for Diagnosis (Fibrositis Circumscripta? Paraffinoma?). Presented by DR. MARJORY HARDY (by invitation), Norristown, Pa.

L. W., a Negress aged 52, was first seen on Jan. 5, 1940. On the outer aspect of the upper part of the left arm the patient had an infiltrated plaque, 12.7 cm. long and 6.3 cm. wide. The skin over the lesion was intact. She stated that the area had been present two years. There was no history of injury to the arm and no history of infections at the site. The area is somewhat smaller and definitely less infiltrated since the patient has received 0.32 Gm. of ammonium chloride three times a day. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. FRED D. WEIDMAN: I was impressed by the warmth of the lesion. This suggests a continued inflammatory process, which would hardly fit in with scler- edema adultorum. The condition would have to be a remarkably localized example of that disease, and I could not get any history of a febrile state at the onset. I doubt that trichinosis would be the cause. A biopsy should be performed.

DR. MORRIS MARKOWITZ: I suggest fibrositis circumscripta. The skin covering the lesion seems to be free.

DR. BERTRAM SHAFFER (by invitation): In Weber's original article on relapsing nonsuppurative nodular panniculitis (Weber, F. P.: A Case of Relapsing Non-suppurative Panniculitis Showing Phagocytosis of Subcutaneous Fat Cells by Macrophages, *Brit. J. Dermat.* 27:301, 1925), he mentioned cases of localized fibrositis of this type. I think this condition would easily fall into this category.

DR. JOSEPH V. KLAUDER: The lesion appears to me to be attached to the skin and not to involve the muscle.

DR. VAUGHN C. GARNER: I think one must consider the possibility of paraffinoma, though I know the patient states that she has never received injections of paraffin.

Correspondence

SUPERFICIAL NONINFLAMMATORY LESIONS OF THE FEET

To the Editor —I should like to make the following observations relative to the article by Dr Sutherland-Campbell, on "Superficial Noninflammatory Lesions of the Feet" (ARCH DERMAT & SYPH 41 6 [June] 1940) The conditions described have been repeatedly observed by most dermatologists but have not been reported The same situation existed some years ago relative to Shamberg's disease The interesting point in this report is the finding of a fungous structure

I have personally observed and prescribed for a number of these conditions and have invariably found them associated with warts The wart, however, has not been the usual plantar type but has consisted of closely grouped lesions, the centers of which have been filled with a crumbly material which can be pricked out entirely with a knife When this has been done the floor of the lesion is flat and does not have the bleeding points of the usual verruca vulgaris These lesions have shown an unusual resistance to heavy roentgen therapy, and if they have disappeared they reappear surprisingly in the same location They also resist other forms of destructive treatment to a considerable degree I have called these lesions "aggregate warts" If these lesions occur on the sole, in the presence of considerable moisture, particularly in contact with composition and nonabsorptive inner soles, they assume the characteristics of the condition described by Dr Sutherland-Campbell When this form has been assumed it approaches the state of porokeratosis I consider that this form is simply a modification of the wartlike type due to pressure and maceration

I have found that these conditions respond to compound ointment of benzoic acid N F, but they will also respond to a considerable degree to dry footwear

It is interesting that Dr Sutherland-Campbell has demonstrated a fungus within the lesion, and if this can be proved to be the causative organism the present conception of this particular form of wart will probably have to be modified

MERLIN T-R MAYNARD, M D, San Jose, Calif

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MASSIVE ARSENOTHERAPY IN EARLY SYPHILIS BY THE CONTINUOUS INTRAVENOUS DRIP METHOD

THE PRELIMINARY WORK WITH NEOARSPHENAMINE

GEORGE BAEHR, M.D.
NEW YORK

This meeting has been called in order to review the results of massive dose chemotherapy of syphilis by means of the intravenous drip. The observations to be reported represent an experience with more than 375 male patients with the primary or secondary stage of syphilis.

Rapid sterilization of the body by massive arsenotherapy was the primary aim of Paul Ehrlich. Later, others also attempted to administer amounts of Ehrlich's chemotherapeutic agent comparable to those which are being reported today, but the dangers involved made it necessary to revert to small divided doses given intravenously every five days for one to two years. This prolonged method of therapy results in a loss of 40 to 80 per cent of clinic patients while they are still in the communicable stage of the disease and can continue to spread infection to others. The disease has therefore continued to spread annually to several hundred thousand persons in this country, despite the availability of a specific remedy for thirty years.

In 1931 Hirshfeld, Hyman and Wanger,¹ working in the laboratories of the department of pharmacology, Columbia University College of Physicians and Surgeons, under Professor Charles C. Lieb, described the syndrome of "speed shock" in laboratory animals following rapid intravenous injections. The work suggested that the reactions following intravenous administration of many therapeutic substances, which are called nitritoid crises, anaphylactoid reactions and hemoclastic or colloidoclastic disturbances, might in fact be "speed shock" and might represent a manifestation of a technical error rather than a specific

This and the following papers were read at a Conference on Massive Arsenotherapy in Early Syphilis by the Continuous Intravenous Drip Method, called by the Commissioner of Health of the City of New York, Dr. John L. Rice, at the Mount Sinai Hospital, New York, on April 12, 1940.

1. Hirshfeld, S.; Hyman, H. T., and Wanger, J. J.: Influence of Velocity on Response to Intravenous Injections, Arch. Int. Med. 47:259 (Feb.) 1931.

pharmacologic effect of the injected chemical. It was demonstrated by these authors that "speed shock" could be prevented by an intravenous drip velocity which could be regulated so that fluids were introduced into the body at a rate of approximately 2 or 3 cc (60 to 90 drops) per minute. It was also observed that this slow rate of flow also permitted the introduction of remarkably large amounts of highly toxic substances, such as anaphylatoxin, histamine and even heavy metals, with complete impunity.²

In 1932 Dr. Louis Chargin, syphilologist of the Mount Sinai Hospital and the New York City Department of Health, proposed that the slow drip method might permit the introduction of large amounts of an arsphenamine in the treatment of syphilis. With the authorization of the trustees of the Mount Sinai Hospital, this work was begun in my service seven years ago (1933).

In the first series, 25 patients suffering from recently acquired syphilis were treated by Drs. Chargin, Leifer and Hyman.³ Four to 4.5 Gm of neoarsphenamine was administered in five days, an amount equal to that ordinarily given in three months. No other form of therapy was used, the patients being followed periodically during the succeeding years. At the end of five years, 15 of the 25 persons in the original group were still under observation. Twelve had remained well and their blood and spinal fluid had given negative serologic reactions for more than five years. These twelve and the following patient can therefore be declared to have been cured.⁴

One man became reinfected after having had completely negative Wassermann reactions of the blood and spinal fluid for three years and two months. Fortunately, he reported promptly when the new primary lesion was still in the seronegative stage. The lesion had appeared after the proper incubation period following exposure to a woman who was found to have an active infection. It was at a new site on the penis, and spirochetes were easily demonstrable by the dark field method. Treatment was postponed until after the Wassermann reaction had become positive under observation and after a typical secondary rash had

2 Hyman, H. T., and Hirshfeld, S. Therapeutics of Intravenous Drip, *J. A. M. A.* **100** 305 (Feb. 4) 1933. Hyman, H. T., and Touroff, A. S. W. Therapeutics of Intravenous Drip. Further Observations, *J. A. M. A.* **104** 446 (Feb. 9) 1935.

3 Chargin, L., Leifer, W., and Hyman, H. T. Studies of Velocity and Response to Intravenous Injections. Application of Intravenous Drip Method to Chemotherapy as Illustrated by Massive Doses of Arsphenamine in Treatment of Early Syphilis, *J. A. M. A.* **104** 878 (March 16) 1935.

4 Hyman, H. T., Chargin, L., and Leifer, W. Massive Dose Arsenotherapy of Syphilis by Intravenous Drip Method. Five-Year Observations, *Am. J. M. Sc.* **197**:480 (April) 1939.

appeared. There is therefore no question that this condition was a reinfection, which constitutes unequivocal evidence that the five day treatment three years before had effected a complete cure.

Another man had a similar experience one year and seven months after treatment and apparent cure, but because of the shorter time interval my colleagues and I have labeled this case a possible failure. The fifteenth member of the group, a hospital orderly, who had insisted on administering a bismuth compound to himself, gave a history of having had a 2 plus reaction in the blood on one occasion, although both the blood and the spinal fluid reacted negatively during our observations before and after that time. His case was also counted as a possible failure.

It was tentatively concluded that permanent and complete cure was possible with five days' treatment and that this technic might provide the means for the more rapid eradication of the communicable stage of syphilis. The observations, if confirmed, offered a new vista for the control of syphilis, but caution was advised until a larger experience had demonstrated its safety.

After unsuccessful efforts had been made during 1935 and 1936 to obtain the necessary financial support for continuing the work under the supervision of a distinguished committee of experts, the importance of the problem to public health was appreciated by Mr. David M. Heyman, a member of the Board of Health. With his assistance, the funds required for two years were obtained from the New York Foundation, assisted during the first year by the Friedsam Fund and during the second year by the John and Mary Markle Foundation. The money was administered by the Committee on Neighborhood Health Development, under the direction of Mr. Kenneth Widdemer. Funds for the support of the original work had been contributed by the late Ernst Rosenfeld, at that time a trustee of the Mount Sinai Hospital.

After financial support had been received, active work was resumed in the winter of 1937 at the Mount Sinai Hospital, with the encouragement and active support of Mayor LaGuardia, Commissioner Rice and Surgeon General Parran. With their assistance, a committee was assembled to supervise all details of the project, under the chairmanship of Dr. Charles C. Lieb. The committee included the following persons:

Representing the Department of Health of the City of New York:
Dr. John L. Rice, Commissioner
Dr. Theodore Rosenthal, Director of the Bureau of Social Hygiene

Representing the United States Public Health Service:
Dr. John F. Mahoney, United States Marine Hospital at Staple-
ton, N. Y.

Representing the American Social Hygiene Association

Dr Walter Clarke, Medical Director

Representing the Department of Medicine, Columbia University

Dr Walter W Palmer, Professor of Medicine

Representing the Department of Medicine, Cornell University

Dr Eugene DuBois, Professor of Medicine

Representing the Mount Sinai Hospital

Dr George Baehr

Patients with primary or secondary syphilis selected by members of the department of health were admitted to a six bed ward in my service at the Mount Sinai Hospital, where the treatment was administered by the three investigators, Drs Hyman, Chargin and Leifer. Two or three days after completion of the treatment the patients were transferred alternately for follow-up studies to Dr Bruce Webster at New York Hospital or to Dr Evan Thomas at Bellevue Hospital.

Under the careful control of the committee, the original investigators treated a second group of 86 patients with neoarsphenamine. The observations on the first series, treated in 1933, were confirmed. As reported by them before the American Medical Association in 1939⁵ and by them and me before the Association of American Physicians,⁶ about 86 per cent of the patients who continued under observation after the five day course of treatment remained clinically well, with negative serologic reactions of both blood and spinal fluid.

After this report was published, the serologic reactions became completely negative in 4 cases in which results were still pending, and these cases may therefore be added to the group with satisfactory results. Of the 78 patients followed, 71 now have negative serologic reactions of the blood and the spinal fluid and are clinically well. The percentage of favorable results with neoarsphenamine is therefore 91 per cent.

Of the entire series of 86 patients to whom the treatment was given, 1 died and 7 disappeared from observation shortly after the treatment was concluded. Of the 7, 2 were never seen again after discharge from the hospital, 4 were lost after paying only one visit to the follow-up clinic two weeks after discharge, and 1 was seen for the last time six weeks after discharge, at which time the Wassermann reaction of the blood was fading rapidly. If all 7 patients who were lost shortly after

5 Hyman, H T , Chargin, L , Rice, J L , and Leifer, W Massive Dose Chemotherapy of Early Syphilis by Intravenous Drip Method, *J A M A* **113** 1208 (Sept 23) 1939. Hyman, H T , Chargin, L , and Leifer, W Massive Dose Arsenotherapy of Syphilis by Intravenous Drip Method, *Am J Syph, Gonorr & Ven Dis* **23** 685 (Nov) 1939.

6 Baehr, G , Hyman, H T , Chargin, L and Leifer, W Massive Dose Arsenotherapy of Syphilis by the Intravenous Drip Method, *Tr A Am Physicians* **54**:25, 1939.

completing treatment are regarded as possible failures, an unwarranted assumption, it would reduce the percentage of favorable results to 83 per cent. As all 7 patients had completed the full course of treatment, however, it is reasonable to assume that the percentage of favorable results is equal to that of the group of 78 that were followed.

Toxic phenomena, chiefly polyneuritis, frequently followed the use of neoarsphenamine. Although usually mild, they were sufficiently disturbing to warrant the trial of another, less toxic arsenical. In the fall of 1938, after the only treatment fatality in the two series of 111 patients treated with neoarsphenamine (cause of death, hemorrhagic encephalitis), further work with this arsenical was discontinued and mapharsen⁷ was substituted.

The use of mapharsen was begun in October 1938. About 265 patients have now been treated with this preparation. Toxic symptoms have been almost wholly eliminated. In his report, Dr. Chargin will

Experiences with Neoarsphenamine: Results of Massive Arsenotherapy by Intravenous Drip Method for Five Days

Series	Follow-Up Study	Number of Cases	Seronegative Reactions and Well		Failures: Clinical or Serologic Relapse	Doubtful Seropositive Results	Maximum per Cent Failure
			Number	Per Cent			
1	6 yr.	15	13*	86.6			
2	2 yr.	78	71	91.0	1†	1	13.4
Total.....		93	84	90.3	4	3†	9.0
							9.7

* One definite reinfection after three years.
† One questionable reinfection.

compare them with those observed after neoarsphenamine. The follow-up period is still too short to permit any final statistical evaluation, but the therapeutic results seem to be comparable to those obtained with neoarsphenamine. They will be reported in detail by subsequent speakers (Drs. Hyman, Webster and Thomas).

Before concluding, appreciation must be expressed to those who have generously contributed their assistance: Dr. Harry Sobotka, chemist to the Mount Sinai Hospital, for the analyses of arsenic in the blood and the excreta; Dr. Louis Soffer, for tests of hepatic function, and Dr. Nathan Rosenthal, for the hematologic observations. The New York City Department of Health, through Commissioner John L. Rice and the director of the Bureau of Social Hygiene, Dr. Theodore Rosenthal, has placed its large clinical material freely at our disposal. The trustees and the executive director of the Mount Sinai Hospital have contributed all necessary hospital facilities without stint.

7. The hemialcoholate of 3-amino-4-hydroxyphenylarsineoxide hydrochloride.

The arduous follow-up work, which included examining patients usually at two week intervals, was the responsibility of Dr Bruce Webster and Dr Evan Thomas and their staffs at New York Hospital and Bellevue Hospital. At each visit samples of blood were taken in triplicate, one being examined at the local hospital, one sent to Mr Koopman, chief serologist of the New York City Department of Health, and the third sent to Dr John Mahoney at the United States Marine Hospital on Staten Island. The work which is now to be reported is therefore the combined effort of a large group of persons. The follow-up observations were made by experts in two independent institutions which were not responsible for the treatment. The Wassermann tests and other serologic work were carried out independently in three laboratories, in two of them by quantitative titration methods.

It is the opinion of members of the committee which has supervised the work that the relative lack of toxicity observed with mapharsen warrants a trial of this therapeutic technic in other well organized hospitals. Modifications and improvements in the technic will undoubtedly be made by others. Although the additional use of a bismuth compound and other effective therapeutic agents might have resulted in even better therapeutic results, they were omitted in order that the effectiveness of the five day treatment with the arsenical alone might be determined. Without such adjuvants, 15 per cent of the patients may require a second five day course of treatment after an interval of six months.

The committee and the Commissioner of Health have invited only a selected group of experts to this conference in order that trial of the method may be limited at present to well equipped hospitals. The technic cannot be recommended for general adoption until a larger volume of experience under careful hospital supervision has been accumulated and the necessity for the supplementary therapeutic agents has been determined. It is already apparent that the method offers encouraging possibilities for the prompt control of syphilis in the highly communicable stage.

MASSIVE ARSENOTHERAPY IN EARLY SYPHILIS BY THE CONTINUOUS INTRAVENOUS DRIP METHOD

TECHNIC

WILLIAM LEIFER, M.D.
NEW YORK

The apparatus employed in the intravenous drip is packed and autoclaved in a special container, devised by Dr. Joseph Turner, director of the Mount Sinai Hospital. The feature of this box is a slot containing perforations which are open while in the autoclave and closed at all other times to prevent contamination.

Each set consists of a gravity flask and two lengths of translucent rubber tubing connected by a Murphy drip. The longer strip of tubing is attached to the gravity flask; the shorter, to an adaptor which fits a standard 20 gage, $1\frac{1}{2}$ inch (3.8 cm.) needle.

The drugs are dissolved in a solution of triple-distilled water containing 5 per cent dextrose. Because of instability, the neoarsphenamine solutions were made up at hourly intervals, as has been previously described. In the present work, the content of an ampule containing 60 mg. of mapharsen has been dissolved in 600 cc. of the diluent. Where facilities are not available for the preparation and sterilization of solutions, commercial sets of the type approved by the Council on Pharmacy of the American Medical Association may be purchased ready for use. Dr. Bernard I. Kaplan, internist at Sing Sing Prison, has employed the latter technic, simply adding the drug to the commercial set. The solution of mapharsen is stable. At present four doses of the drug in the diluent are given without intermission each day, so that each patient receives 240 mg. of mapharsen in 2,400 cc. of 5 per cent dextrose solution, which contains 120 Gm. of the sugar. The rate of flow is approximately 3 cc. a minute. Ordinarily the drip is set up about 8 a. m., and the full dose has been injected by the end of ten to twelve hours. At the end of this period the needle is withdrawn, treatment being discontinued during the night but resumed the next morning. This procedure is carried out daily for five consecutive days until a total of 1,200 mg. of the drug has been administered in 12,000 cc. of

Read at a Conference on Massive Arsenotherapy in Early Syphilis by the Continuous Intravenous Drip Method at Mount Sinai Hospital, New York, April 12, 1940.

diluent, containing 600 Gm of dextrose. The total arsenic content is approximately 360 mg.

The choice of the vein is an important consideration. In the earlier work, in 1933, the site of injection was the cubital fossa. This required splinting of the arm, which not only interfered with the care of the patient but was uncomfortable, the pressure of the splint occasionally leading to traumatic neuritis. Throughout the recent work, the elected site for the insertion of the needle has been a vein on the forearm between the elbow and the wrist. This permits free movement of the elbow, and no splint is required, the patient may assist in feeding and in nursing procedures, such as the use of the bedpan, there is less danger of dislodging the needle from this site than at the bend of the elbow, where motion occurs. It is desirable to insert the full length of the needle, up to the hub, for firmer anchorage. The right and the left arm are used alternately for the injection procedure. Usually a vein can be employed again after a rest of twenty-four hours.

Local disturbances are infrequent. It was thought that the slow injection of mapharsen would cause pain in the arm, but this has been rarely encountered. Infiltrations have occurred, but with the greatest rarity—in less than 0.5 per cent of the patients treated. Traumatic neuritis has been absent since the discontinuance of the use of arm splints. Local infection has never been seen.

The nursing problem during the period of treatment consists of the preparation of fresh solution for each patient at the end of two or three hours and the refilling of the gravity flask. Meals are served on the ordinary bed tray. Patients can feed themselves. They are also capable of handling the urinal but, naturally, must be assisted somewhat in the use of the bedpan. The latter disturbance may be prevented by having the patient evacuate or have an enema during the evening, when treatment has been discontinued.

The patients are given a high calory diet, rich in starches and carbohydrates. The majority of the patients read, listen to the radio or play cards during the day. In the evening, after discontinuance of therapy, they may get out of bed. They suffer little or no discomfort. Many of them register a gain in weight of as much as 10 pounds (4.5 Kg). This gain in weight is not due to any appreciable edema but may be explained by the fact that most of these patients otherwise undernourished are so well treated with regard to food and nursing care.

The routine examinations consist of the following:

- 1 Daily urinalysis, including determination of urobilin
- 2 Determinations of the urea nitrogen content of the blood and the icterus index at the beginning and at the termination of treatment
- 3 Complete blood count, including that of the platelets, at the beginning and at the termination of treatment

4. Complete physical examination on admission.
5. Serologic examinations made in three different laboratories (these include the Kolmer, Kline diagnostic, Kline exclusion, Kahn standard and titered Wassermann tests).
6. Dark field examination of material from all open sores.
7. Estimations of renal function by determination of the specific gravity of the urine.
8. Special tests of hepatic function by the bilirubin method.
9. Studies of the excretion of arsenic in the urine and in the stool and its concentration in the blood (these studies have been made on only a limited number of consecutive patients).

With the exception of 1 young woman, all the patients treated have been males. The reasons for this were administrative and practical, first, that a male ward was made available for the study and, secondly, that it was far easier to obtain patients with early syphilis among males than among females. A little more than 50 per cent of the patients were white, 2 were Chinese and the remainder were Negro. Over 70 per cent of the patients fell into the age group of 20 to 40, the youngest patient being 13 and the oldest 56.

MASSIVE ARSENOTHERAPY IN EARLY SYPHILIS BY THE CONTINUOUS INTRAVENOUS DRIP METHOD

TOXICOLOGIC MANIFESTATIONS

LOUIS CHARGIN, M D

NEW YORK

This communication deals, in brief, with the toxic manifestations observed in 270 patients treated with mapharsen in various dosages by the drip method of therapy

The toxic manifestations in 111 patients treated with neoarsphenamine have already been reported¹ In the neoarsphenamine series, there were one fatality due to hemorrhagic encephalitis and a rather high incidence of polyneuritis (38 per cent) This led us to the substitution for neoarsphenamine of another arsenical, namely, mapharsen, which we had reason to believe might prove less toxic and perhaps equally efficacious therapeutically, if we were to judge by our experience with a large series of patients with early syphilis treated by the routine method

In the 270 patients for whom treatment with mapharsen has been completed, there has been no death due to the treatment In 1 patient in the series hemorrhagic encephalitis developed, which will be discussed later With this single exception there have been no important toxicologic manifestations in any of the patients

The primary or Heixheimer fever was also observed in the present series This reaction consists of a brisk rise in temperature on the first day of treatment Usually there is but a single spike and the temperature returns to about normal the next morning, at which time treatment is resumed This febrile reaction has no serious connotation and does not interrupt the progress of the treatment It was observed in 62 per cent of the patients receiving neoarsphenamine and in approximately 40 per cent of the present series

Secondary fever, frequently associated with or followed by toxicoderma, appears toward the latter part of therapy or after its termination

Read at a Conference on Massive Arsenotherapy in Early Syphilis by the Continuous Intravenous Drip Method at Mount Sinai Hospital, New York, April 12, 1940

1 Hyman, H T , Chargin, L , Rice, J L , and Leifer, W Massive Dose Chemotherapy of Early Syphilis by the Intravenous Drip Method, J A M A 113 1208 (Sept 23) 1939

This occurred in 64 per cent of the neoarsphenamine series and in only 13 per cent of the mapharsen series. The secondary fever may appear without toxicoderma, and, similarly, toxicoderma may appear without febrile reaction. The toxicoderma is usually morbilliform, rarely urticarial. It occurred in 45 per cent of the neoarsphenamine series and in approximately 11 per cent of the present series. These eruptions should not be confused with the major dermatitides due to arsphenamine. They are not of serious import and do not sensitize the patients to future injections of remedies of the arsphenamine group, since a number of the patients who had toxicoderma have been treated again without any untoward cutaneous reactions.

Peripheral neuritis of a significant degree was not observed by us in this series, although minor paresthesias, never significant, may occur after the patient's discharge from the hospital. It may be stated in passing that in the neoarsphenamine series the injection of thiamine chloride vitamin B₁ proved valueless as either a prophylactic or a therapeutic agent; also, the administration of vitamin C in preventing the secondary fever or the toxicodermas proved fruitless.

It is interesting to observe that the nitritoid reaction, which occurs in 0.1 to 0.5 per cent of all patients to whom injections of neoarsphenamine or arsphenamine are given, was not observed in a single patient in either series, and we have now given almost two thousand injections of massive doses. The intravenous drip method has eliminated this reaction. This experience strongly suggests that the nitritoid crises and colloidoclastic and anaphylactoid phenomena are merely clinical manifestations of "speed shock," as first suggested by Dr. Hyman.

Renal function during treatment has been carefully observed and studied. With the exception of transitory albuminuria in an occasional case, there has been no evidence of any significant disturbance of renal function.

We have studied the effect of massive dose therapy with the arsenicals on the liver. In addition to observations for clinical jaundice, daily examinations of urine for urobilin have been made. The icteric index has been followed, and special tests for bilirubin retention have been performed by Dr. Louis Soffer and his associates. In this series there were 2 instances of transitory jaundice while the patients were in the hospital. Occasionally a slight increase in the excretion of urobilin or in the icteric index has been found later, but this has been transitory and, apparently, of no important significance. It may also be noted that in a number of instances the icteric index before treatment was found to be above normal, as high as 15. This perhaps is indicative of mild hepatic damage due to syphilis. In most of these cases after the termination of treatment the icteric index fell to normal levels.

In 1 young man toxic hepatitis developed six months after the completion of therapy. This 26 year old native Virginian began his experience with hard liquor at the age of 10 years. By his eighteenth year he was a confirmed drinker, taking more than a quart (946 cc) of hard liquor daily in addition to quantities of beer. He continued this practice before and after discharge from the hospital, to which he was admitted with a syphilitic infection of four months' duration. For the infection he received a total of 0.7 Gm of mapharsen, without having the slightest difficulty. Six months later he was readmitted to the hospital, because of persistently positive results of serologic blood tests. On this occasion he received 1.2 Gm of mapharsen in five days, again tolerating it well. Six months after this (in the interval he continued his usual custom of taking a quart of hard liquor per day) he returned to the clinic for a check-up. It was then discovered that he had jaundice. He was admitted to the hospital for the third time, now with the diagnosis of toxic hepatitis. Drs. Soffer and Sager, after careful consideration, expressed the view that the arsenic may have played a role in the production of the hepatitis but that to alcohol must be attributed the greater role. After ten days under appropriate treatment he was discharged practically well.

Through the cooperation of Dr. Nathan Rosenthal, the effects of massive dose arsenotherapy on the hemopoietic system have been observed. In the neoarsphenamine series there were 2 instances of thrombopenic purpura. The condition in 1 case was idiopathic and and was cured by splenectomy, in the other definite sensitivity to arsenic was found. In the present series of patients treated by mapharsen no untoward effects on the formed elements of the blood have been noted.

Cerebral complications and the major dermatitides remain the bugbear of arsenotherapy. In the neoarsphenamine series there were 2 instances of hemorrhagic encephalitis, in 1 of which the condition proved fatal. In the present, much larger series, consisting of 288 courses of treatment, there have been 3 persons with cerebral symptoms. Two of these had mild symptoms, 1 of them had a single convulsion and promptly recovered, and the second was dazed for a short time and completely recovered. Neither required active treatment. The third, a white man aged 26, was admitted with the diagnosis of seropositive primary syphilis. General examination revealed that he was suffering from chronic rheumatic cardiovascular disease affecting the aortic and mitral valves, but the process was inactive. He received 1.2 Gm of mapharsen in five days. He took the treatment well. On the seventh day, i. e. on the second day following completion of treatment, headache developed, and soon thereafter there was a convulsion, which was followed by five additional attacks in four hours. He lapsed into stupor for forty-eight hours. With repeated lumbar puncture, intravenous administration of a 50 per cent solution of sucrose and paraldehyde sedation, he completely recovered in five days. He is now in perfect condition, two months after the episode.

One must forever be on guard for cerebral complications in the course of any form of arsphenamine therapy. The important early

symptoms include severe headaches, drowsiness, persistent vomiting, dizziness, changes in personality, confusion and convulsions. If they are recognized in time and prompt treatment is instituted, the outlook is not as bad as is usually assumed. We regard three measures as important in therapy: (1) repeated lumbar puncture, (2) sedation (for this purpose paraldehyde was found to be superior to other drugs) and (3) dehydration, by means of frequently repeated intravenous injections of 50 per cent sucrose. We doubt, incidentally, the value of sodium thiosulfate either for this condition or for the arsphenamine dermatitides.

Hemorrhagic encephalitis has been responsible for 1 death and for 1 serious illness in our entire series. This is an incidence of 2 in 399

*Comparison of Toxic Effects in Neoarsphenamine and in Mapharsen Series
(as of May 21, 1940)*

	Neoarsphenamine		Mapharsen	
	Number	Per Cent	Number	Per Cent
Total treatment courses (399 treatment cases).....	111	..	288	..
Primary fevers.....	69	62	116	40
Secondary fevers.....	71	64	36	12
Toxicodermas.....	50	45	33	11
Dermatitis exfoliativa.....	1*	0.9	0	..
Blood dyscrasias.....	0	..	0	..
Renal damage.....	0	..	0	..
Jaundice.....	4	3.6	2	0.7
Peripheral neuritis.....	39	35	5	1.6
Cerebral symptoms (total).....	2	1.8	3	1.04
Hemorrhagic encephalitis.....	1	0.9	1	0.34
Single convulsion.....	1	0.9	1	0.34
Disorientation.....	0	..	1	0.34
Fatality.....	1	0.9	0	..

* Received sulfanilamide for complicating gonorrhea.

courses of treatment (this figure includes retreatments). From what we are able to gather from the literature, it seems that the number of instances of this complication in our series is not excessive. Cole,² for example, reported 12 deaths due to treatment in 1,212 cases, or 1 in 100. Half of the deaths were due to hemorrhagic encephalitis, that is, a ratio of 1 in 200. The cerebral symptoms, in Cole's experience, in 5 of 6 patients occurred with four or fewer injections of the arsenical. The inference seems warranted that hemorrhagic encephalitis is a manifestation of sensitivity rather than of overdosage. This viewpoint was also emphasized by Glaser, Imerman and Imerman³ in their analysis of 158 cases of hemorrhagic encephalitis. The experience

2. Cole, H. N., and others: Toxic Effects Following Use of Arsphenamine, J. A. M. A. **97**:897 (Sept. 26) 1931.

3. Glaser, M. A.; Imerman, C. P., and Imerman, S. W.: So-Called Hemorrhagic Encephalitis and Myelitis Secondary to Intravenous Arsphenamines, Am. J. M. Sc. **189**:64 (Jan.) 1935.

in the United States Navy, as reported by Phelps,⁴ shows that there were 27 deaths among approximately 6,730 patients given 175,000 doses of arsenicals, or 1 treatment death per 264 cases. Accordingly, the incidence of hemorrhagic encephalitis with massive dose therapy is no greater than with routine treatment.

Statistics that can be compared with ours, dealing with the less severe toxic phenomena, are not available. Our patients have been subjected to the closest scrutiny over extended periods of time and periodically observed. Such observation is not practicable in the average clinic for ambulatory patients, consequently there are not many publications for comparison. It is obvious that in clinical practice there are few observations on primary or secondary fever. In the average clinic many patients are lost from observation, and such minor toxic phenomena as develop may escape notice or be ignored altogether. Also patients may seek treatment at institutions other than the original one. From long personal experience, however, in the treatment of ambulatory patients with syphilis, I am inclined to believe that the minor toxic manifestations observed in clinic practice do not much differ from those we have encountered with the drip method of therapy.

Figures on treatment mortality which are available, however, and which again are modified by the fact that it is not easy in ambulatory forms of therapy to ascertain deaths which may have occurred in other institutions, show convincingly that our experiences are no worse, if not better, than those recorded in the literature. In the naval service dealing with healthy men there was 1 treatment death per 264 patients. In the Cole series there was 1 death in 100 patients. In the present group, thus far, there has been 1 death in 399 patients. Therefore, we feel that this method of therapy, with the drug now in use, is as safe as any.

Finally, it should be stated that we have not observed a single case of any of the major dermatitides due to the drip therapy with mapharsen.

4 Phelps, J. R. Reactions Incidental to the Administration of 191,778 Doses of Neoarsphenamine and Other Arsenical Compounds in the United States Navy, U. S. Nav. M. Bull. 27:205 (Jan.) 1929.

MASSIVE ARSENOTHERAPY IN EARLY SYPHILIS BY THE CONTINUOUS INTRAVENOUS DRIP METHOD

CLINICAL CONSIDERATIONS

HAROLD THOMAS HYMAN, M.D.
NEW YORK

TREATMENT WITH NEOARSPHENAMINE

In May 1939 at the meeting of the American Medical Association in St. Louis I reported, in collaboration with Commissioner Rice, the course of a group of 86 patients with primary or early secondary syphilis who received, by means of the intravenous drip, 4 Gm. of neoarsphenamine over a period of five days. We are now able to report further observations that have been collected in the eleven months that have elapsed.

Patients Lost from Observation.—We have been unable to establish contact with any of the 7 patients previously reported as having lapsed from follow-up observation. Two of these patients were never seen after they were discharged from the hospital; 3 made one visit to the follow-up clinic, and 1 made two visits. In massive dose chemotherapy the situation of the patients who allow treatment to lapse, since the latter, that of those who allow routine treatment to lapse, both to the community and to themselves. In our series treatment was completed on having had insufficient dosage, are a greater menace both to the community and to themselves. In our series treatment was completed on these delinquents, and since the condition in 90 per cent of the followed patients has cleared, it is fair to assume that the vast majority of the patients who have lapsed from the follow-up studies have progressed satisfactorily, even though the outcome, so far as our records are concerned, is unknown.

Deaths Due to Treatment.—The single fatality from therapy was that of the man who died of hemorrhagic encephalitis. Since the last report, 1 patient among those whose serologic reactions became negative has died of carcinoma of the stomach.

Completed Records.—Subtracting the 1 death due to the treatment and the 7 patients who were lost from observation shortly after completion of the treatment, 78 patients remain for whom complete records are available.

Read at a Conference on Massive Arsenotherapy in Early Syphilis by the Continuous Intravenous Drip Method at Mount Sinai Hospital, New York, April 12, 1940.

pleting treatment, and concerning whom no opinion can be expressed, there are 78 completed cases to be discussed

Failures—There were 4 failures, as previously reported, the percentage approximating 5. Three of the 4 patients suffered an infectious relapse and 1 a serologic relapse. The spinal fluids of 3 of the patients were completely normal, despite the positive reaction of the blood. The fourth patient was a morphine addict whose wife had active syphilis at the time he showed an infectious relapse. The reaction of his spinal fluid was positive. In the entire series of patients treated, this is the only time that a positive reaction of the spinal fluid has been encountered.

Each of these patients has been retreated by routine methods, since at the time we were not committed to the policy of retreatment by massive dose chemotherapy. During the eleven months since the last report, there has not been a single failure to add to the unsuccessful group.

Results Pending—The course in 3 patients must be regarded as incomplete and the results as pending. The serologic reactions in each of these were tending toward reversal when the patients were last seen. It is still possible that at least 2 of them may return for observation at some future time.

Serologic Reversal—The remaining 71 patients have negative serologic reactions and are symptom free and clinically well. They constitute 82 per cent of the entire group of 85 survivors, including those who were lost from the follow-up study and those in whom results are pending, and 91 per cent of the group that was followed, including the 3 patients with pending results.

Seventy-three tests of spinal fluid were made for 66 of the patients, and all the reactions were negative. In 5 instances we have been unable as yet to obtain a specimen of spinal fluid. Serologic reversal was achieved in an average of twelve weeks. It is interesting to observe that in some instances serologic reversal did not occur until beyond forty weeks. The total span of observation to date approaches two years. Many of the patients have had more than fifteen negative serologic reactions.

Comparison between the clearing of the results of the complement fixation test and that of the more sensitive flocculation test shows a lag in the clearing of the latter that amounted to an additional one or two follow-up visits.

The neoarsphenamine series may be summarized by the statement that against a single treatment death and a high incidence of peripheral neuritis there was a record of serologic reversals in excess of 80 per cent of the entire group and in excess of 90 per cent of the patients followed. The definitive treatment failures total 5 per cent. These

are the results of a five day treatment with a total of 4 Gm. of neoarsphenamine, no other specific therapy having been given to any patient at any time.

TREATMENT WITH MAPHARSEN

After the death due to treatment, the members of the committee decided to continue massive dose chemotherapy by the intravenous drip method but to substitute for the neoarsphenamine an arsenical that might be less toxic and more stable, even if the therapeutic efficacy were not so great. For this purpose mapharsen was chosen.

The problem of optimal dosage was an immediate concern. Since mapharsen is commonly used clinically in the ratio of 1 to 10 with regard to neoarsphenamine—that is, 60 mg. as against 600 mg.—a beginning dose of 10 per cent of the 4 Gm. dose of neoarsphenamine, or 400 mg., of mapharsen was selected.

It soon became obvious that the toxicity of mapharsen was so slight that increased dosage could safely be employed. Later, when infectious relapses were encountered, the dose of the drug was gradually and tentatively increased until, by slow stages, the present amount, 1,200 mg., was arrived at, the total being given over the span of five days, as described by Dr. Leifer. Even with this amount of mapharsen, which was three times the amount we originally used, the arsenic content is slightly less than half that of the 4 Gm. dose of neoarsphenamine; the latter, containing approximately 20 per cent of arsenic, possesses 800 mg. of the element, while mapharsen, containing 30 per cent of arsenic, has but 360 mg. of the element per total dose of 1,200 mg.

As a result of the alterations in dosage, the patients treated with mapharsen will be considered in two groups: (1) The group that is under observation at present, which now numbers 100 patients and will be brought up to a total of 125, each of whom has or will have received 1,200 mg. in five days, and (2) the earlier group of the first 157 patients, for whom the dose varied from a minimum of 400 mg. to a maximum of 1,100 mg., the average being 700 mg. or slightly in excess of half of what we now believe to be an optimum and safe dose.

Of the 157 patients in the group that received the smaller dosage:

- 24 received less than 600 mg.
- 30 received approximately 700 mg.
- 27 received 800 mg.
- 49 received 1,000 mg.
- 27 received 1,100 mg.

The earliest patient given the smallest dose was under observation approximately eighteen months ago; the most recent in this series with the larger dose, approximately six months ago. The results of therapy,

which will be indicated now, are necessarily tentative. Those cases reported as failures are, of course, irrevocable. For the group of patients progressing favorably at present only a trend can be reported. Hence, the figures that are to be announced are not definitive, they are subject to interpretation, and they may change appreciably between the present report and the report that will be issued when the committee is satisfied that sufficient follow-up observations have been obtained.

This much, however, can be stated. In the light of our experience with the group treated with neoarsphenamine, in which not a single failure due to treatment has been added during the second year of observation, the later report will probably not differ appreciably from the one to be rendered today. A certain number of patients who are today in the group with pending results may possibly clear as time progresses. Against this, a certain number of persons who are apparently free from infection at present may suffer serologic or infectious relapse, canceling the results that shift toward the more favorable side of the picture.

Through the generosity of the foundations and the far-sighted plans of the Committee, both funds and adequate organization facilities have been guaranteed so that prolonged follow-up observations may be assured.

With these qualifications, it may be stated that of the 157 patients who received an average dose slightly in excess of half of what is now regarded as optimal, the vast majority are pursuing a course which parallels that of the favorable cases observed in the neoarsphenamine series.

With the same type of classification that was agreed to by the committee last spring in the reporting of the neoarsphenamine group, the patients treated with mapharsen in group 1 may be briefly reported on as follows:

Lost from Observation—Sixteen of the 157 patients have not reported to the follow-up clinic for a time sufficient to obtain significant data. We regard these patients as having lapsed from observation, and their number is to be deducted from the total in the group before percentages are calculated. However, since Dr. Webster believes that these patients should be calculated as failures of treatment, I shall also present percentage figures on the total group, i. e., all the patients who lapsed from the follow-up observation being regarded as failures of treatment.

Deaths Due to Treatment—There has been no death due to treatment in the entire series.

Results Pending—The results in 6 patients in the primarily treated group must be regarded as pending. It is impossible today to know whether these patients are going on to serologic clearing or whether

the persistence of the reagin in the serum will continue and place the patients either in the group to be treated again or in the group of acknowledged failures.

Failures.—Twenty-three patients may be included in the group with unfavorable results. Nineteen patients are acknowledged failures, so far as their first course of therapy is concerned. These patients have had either a cutaneous relapse, serum fastness or serologic reversal. None has had positive reactions in the spinal fluid. None has had any visceral manifestations of syphilis, other than the mucocutaneous lesion on the penis. Eleven of these patients have been retreated by a second course of massive dose chemotherapy, since it has become the more recent policy of the committee to retreat immediately those who have a mucocutaneous or serologic relapse, as well as those who exhibit serum fastness at the end of four to six months. This policy somewhat complicates the purity of the experiment. It is done in the interest of the patient, since it is not the desire of the committee to jeopardize the welfare of a single patient for the sake of a purely scientific investigation. There is no dictum that limits massive dose chemotherapy to a single course of treatment. The benefits of the technic would in no way be vitiated if it were necessary to retreat 15 or 20 per cent. of the original group.

Of the 19 patients classified as failures from the first course, 8 were not retreated by massive dose chemotherapy. They were given routine treatment and, so far as this research is concerned, are to be classified as irrevocable failures. Of the 11 who were retreated, 1 has lapsed from follow-up observation; in 5 the results are pending; 3 have had serologic clearing, and 1 has failed to respond in his second course, in that there has occurred a serologic relapse, making a total of 9 (5 per cent) irrevocable failures, the same per cent as in the neoarsphenamine group.

Infectious Relapse or Reinfection.—Four patients present an exceedingly difficult problem. In them, after therapy and serologic clearing, lesions developed on the penis that might be interpreted either as fresh infection or as mucocutaneous relapse. If the latter interpretation is correct, then the 4 patients must be regarded as irrevocable failures. On the other hand, if they suffered reinfection, then they must have been biologically cured and hence should be considered in the favorable group. Syphilologists have correctly set up rigid standards for proof of reinfection. These criteria include several points that are impossible of fulfilment in the course of massive dose chemotherapy. It has seemed to us to be the wiser plan to balance the evidence in favor of and against reinfection so that each may decide in his own mind how best these patients should be classified. It is conceivable that the whole concept

of reinfection may have to be altered in the light of what we shall learn from the course of patients undergoing massive dose chemotherapy

Following the criteria laid down by Stokes and Parran, the following points are in favor of reinfection

- 1 The first infection has been proved
- 2 Serologic reversal has been achieved In 1 patient there was but a single negative reaction, another had two negative reactions, a third had three, and a fourth had eleven
- 3 The spinal fluid was normal in the 1 patient who was subjected to the test
- 4 Each patient gave a definite history of exposure for the second infection
- 5 The infectious source for the second infection of 1 patient was a wife who had active secondary syphilis
- 6 There was a normal incubation period for the second chancre in each of 4 patients
- 7 The second chancre was at a different site in all 4 patients Two of them had multiple lesions Two who had had lesions on the frenum the first time had lesions on the ventral surface the second time
- 8 In 3 of the 4 instances there was no activity at the site of the first chancre
- 9 In each of the 4 instances dark field examination of material from the second chancre gave positive results
- 10 There was satellite adenopathy present with the second chancre
- 11 The Wassermann reaction of the blood, which was negative at the start in each of the 4 instances, changed to positive

Against reinfection and in favor of mucocutaneous relapse the following points may be presented

- 1 The patients did not receive approximately twenty injections of arsenic and twenty injections of a bismuth compound in the course of the first treatment
- 2 Two years did not elapse after the termination of the first course of therapy
- 3 The time interval between the first and the second infection was not two or more years
- 4 The secondary eruption did not appear twenty days after the appearance of the chancre, since these patients were subjected to therapy on the presentation of the lesion
- 5 The Wassermann reaction of the blood was not negative for one year after treatment of the first chancre

6. In 3 instances the spinal fluid was not examined before the time of the appearance of the second lesion.

However these conditions may be interpreted, all 4 patients were retreated by massive dose chemotherapy. Two already have clear serum, and the results in 2 are pending.

One hundred and twelve of the original group of 157 patients have already achieved serologic reversal. An additional 6 patients have had clearing with their second course of treatment. Some of these patients, who have not yet been observed for a sufficiently long time, have had only two or three negative reactions. Others, who have been observed for as long as eighteen months, have had as many as eighteen negative reactions. None of these patients has had any visceral evidence of syphilis. Sixty-nine examinations of spinal fluid have been made, usually some time after the sixth month, and all have given negative results.

Calculating percentage figures by the most severe standards—that is, including as failures of treatment all patients who have been lost from observation, all of those with mucocutaneous relapse, serologic relapse and serologic fastness, those who had second courses of massive dose chemotherapy and the 4 patients suspected of having suffered a reinfection—there are still 72 per cent of the entire group whose course indicates a favorable trend.

If the patients lost from observation within a short time after treatment are excluded, the percentage of those who have secured clearing by their first course of massive chemotherapy is approximately 80 per cent.

If the 4 patients with possible reinfection are added to the 112 who achieved serologic reversal by primary treatment, then the total who secured clearing by primary treatment is 116, or 74 per cent of the original group and 82 per cent of those that were followed.

If to the 112 patients who obtained clearing with the single dose of therapy there are added the additional 6 who obtained it with their second course of treatment, the successful group numbers 118, and the percentage, based on the total group, is 75 and, based on the followed group, 84—the latter figure including 2 of the possibly reinfected patients who secured clearing with the second course of massive dose chemotherapy.

Again, it should be emphasized that these results reported in the early group of patients treated with mapharsen have been achieved with a dose averaging slightly over half of what we now considered to be the optimal safe dosage.

The second group in the mapharsen series consists of 100 patients who have received a dose of 1,200 mg. Since the longest period of

observation for any of these is but six months, there is not much to be said at present that is definitive. However, a preliminary survey of the first 35 patients treated eighteen to thirty-six weeks ago shows that 3 have lapsed from observation, the results in 6 are still pending, 25 have already obtained serologic clearing, and 1 has been retreated because of a tendency toward serologic relapse.

For all of the patients examined while being treated by massive dose chemotherapy, the dark field examinations have given negative results at the end of forty-eight hours. This fact assumes importance from the viewpoint of public health aspects, which will be discussed in further detail by Commissioner Rice.

It is also important to observe at this point, from the public health angle, that 100 per cent of our patients completed their treatment. With ambulatory forms of therapy it has been estimated that a minimal case loss is 25 per cent, the maximum case loss may be as high as 84 per cent, and the average is probably in excess of 50 per cent and closer to 60 per cent. In private practice the case loss is still higher, since the economic factor becomes an important added consideration. With routine forms of therapy the percentage of favorable results, even as reported in the best statistics from the Cooperative Clinical Group, is based not on the number of patients who inaugurated therapy but on those who could be followed for six months or more, the recalcitrant patients being discarded from calculations and menacing the community both from their infectivity and from the fact that the incompletely treated patients, in whom the late degenerative phenomena are more prone to develop, augment the population of hospitals for patients with chronic disease and of welfare institutions.

With the cooperation of Dr. Harry Sabotka, we have carried out studies on the arsenic concentration in the blood in an attempt to determine (1) the necessary arsenic concentration for effective spirocheticidal activity in human beings and (2) the possible explanation of the occasional unsatisfactory result. Whether or not this method is absolute in its accuracy, the calculations are constant.

The arsenic concentration starts at zero. It rises within a few hours to $\frac{1}{10,000,000}$ and this concentration is maintained virtually until midnight, the evening figure being slightly higher and the midnight figure slightly lower. By morning of the second day the concentration is $\frac{1}{20,000,000}$. It rises a few hours after the resumption of treatment to $\frac{1}{10,000,000}$. By evening it is $\frac{1}{5,000,000}$, with a slight fall to $\frac{1}{15,000,000}$ at midnight. On the morning of the third day the concentration is just under $\frac{1}{10,000,000}$. By noon it has risen to $\frac{1}{5,000,000}$. At the termination of all treatment, on the evening of the fifth day, the concentration is

$\frac{1}{3,000,000}$. This is maintained until midnight. The morning following treatment the concentration has fallen to $\frac{1}{5,000,000}$ and it is approximately $\frac{1}{10,000,000}$ for two and three days after the termination of treatment. The final figure is three days after treatment when the concentration has again fallen to $\frac{1}{20,000,000}$.

The most interesting and significant observation is the maintenance of the concentration of between $\frac{1}{5,000,000}$ and $\frac{1}{3,000,000}$ for approximately the entire time that elapses between the institution of treatment on the third day and the day following the termination of treatment. In other words, these concentrations are maintained for the third, fourth and fifth and most of the sixth day, perhaps, approaching ninety-six hours.

Analysis of the patients whose course has not been wholly satisfactory brings out an important therapeutic principle previously described. Dosage, while of some importance, is apparently of much less significance than the time that transpires between the acquisition of infection and the institution of treatment. The importance of this observation with regard to public health will be discussed by Dr. Rice. The fact is that rarely is an unfavorable course observed in, or is secondary treatment required for, patients whose treatment is instituted earlier than the eighth week following infection. These dates, difficult of absolute proof, are substantiated more concretely by the results of the initial serologic examinations. Seronegative patients should never experience difficulty. Patients with a Koopman titration of 7 plus or less or with a Kolmer reading (as done by Dr. Mahoney) totaling 10 or less (43210, for example) may be given a favorable prognosis almost without qualification. Those with a Koopman titration of 10 or more or with a Kolmer titration that exceeds 15 and approaches a maximum of 20 (44444) may have to be retreated because of an infectious relapse. In any event, experience indicates that with a single exception (occurring in a morphine addict exposed to a wife with infectious syphilis), we have not yet seen any person treated by massive dose chemotherapy in whom any visceral manifestations of syphilis have developed other than the mucocutaneous relapses at the site of the origin of the infection.

MASSIVE ARSENOTHERAPY IN EARLY SYPHILIS BY THE CONTINUOUS INTRAVENOUS DRIP METHOD

RESUMÉ OF SEROLOGIC OBSERVATIONS

JOHN F. MAHONEY, M.D.

STATEN ISLAND, N. Y.

In a study of this type reliance must be placed on serologic tests as a means of gaging the effectiveness of therapy after clinical manifestations have subsided. In assisting in the work it was the purpose of the two laboratories which participated to bring to the study a serologic routine which would be soundly critical, which would be as free as possible from the vagaries attributable to the personal equation, which could be maintained without major technical changes throughout the period of observation of the patients and which could be duplicated for a similar study by any laboratory doing good serologic work.

The complete serologic routine consisted of five tests: three flocculation and two complement fixation tests. The serologic laboratory of the New York City Department of Health, under the direction of Mr. John Koopman, reported results obtained with a quantitative complement fixation technic. The Venereal Disease Research Laboratory of the Public Health Service performed a supersensitive flocculation test (Kline exclusion), two flocculation tests set at a diagnostic level (Kahn standard and Kline diagnostic) and a quantitative complement fixation test (Kolmer). All tests of the latter group were carried out in strict accordance with the technical details recommended by the originators, and at three intervals during the study their performances were checked with those of the originators' laboratories. In the testing of spinal fluid the complement fixation methods only were used.

In the patients who have been classified as responding successfully to the intravenous drip therapy, the trend toward serologic reversal was as uniform as could be reasonably expected in view of the variety of tests used and the possible difference in levels of sensitivity which they represented. The duration of the seropositive stage would not be appreciably lengthened or shortened, on the average, if any one of the diagnostic procedures alone was utilized as an index to the end point.

Read at a Conference on Massive Arsenotherapy in Early Syphilis by the Continuous Intravenous Drip Method at Mount Sinai Hospital, New York, April 12, 1940.

The supersensitive Kline exclusion technic would add an average of sixteen days to the duration of the seropositive stage. In the use of this method, however, there is a factor of nonspecificity which is difficult of evaluation. The duration of seropositivity as determined by the complement fixation methods, which has been used in the published reports of the work, may be assumed to represent a fair average of the time required for the clearing of results of the two additional diagnostic flocculation tests.

Of the patients for whom the diagnosis was established by dark field examination in the so-called pre-Wassermann stage of the disease, practically all experienced a serologic upstroke following the therapy. The degree of this response, however, tended to be of low titer and the movement toward reversal to be prompt. In the patients whose serologic response was well established and of high titer at the time of treatment, the trend toward reversal was, as a rule, more protracted.

The follow-up observation of the patients whose diagnoses were established by dark field examinations and who enjoyed rapid serologic reversals after the initiation of treatment will constitute one of the most interesting phases of the study. Although they are generally conceded to be the favorable type for treatment, should a considerable proportion escape serologic and clinical relapse during the five year period, the potential role of the therapy in the control of the disease would be entirely obvious.

Some inconsistencies between the various tests were observed, generally occurring as the concentration of reagin approached the threshold or vanishing point. This is not an uncommon finding in patients who have been vigorously treated by the generally used methods.

From the serologic standpoint alone, the data being accumulated in the study will provide an excellent basis for a comparative analysis of the serologic patterns which are formed by the individual tests as the concentrations of reagin return to the base line. To be accurate this study will have to await a more prolonged observation of the recently treated group of patients.

MASSIVE ARSENOTHERAPY IN EARLY SYPHILIS BY THE CONTINUOUS INTRAVENOUS DRIP METHOD

FOLLOW-UP OBSERVATIONS AT NEW YORK HOSPITAL

BRUCE WEBSTER, M D
NEW YORK

In the evaluation of any experiment of the type just described, the results will fall into three categories. Some will be unqualified successes, others will be rank failures, and still another group will be somewhere between in an inconclusive category. They may fall in this last group for a variety of reasons, such as insufficient observation, controversial findings or results which cannot be readily interpreted. When one is evaluating a problem involving as it does the public health aspects of an infectious disease, with the consequent dangers of exposing others to the infection, one must be overcritical in dealing with this inconclusive group of results, since they represent the real pitfalls of the experiment. Accordingly, with this in mind, I have tended to regard all patients who lapsed from observation while still seropositive as failures. I fully realize that a certain number of these will eventually be cured, but since this cannot be proved, it seems more conservative to regard them as failures. Fortunately, in this experiment the number of such controversial cases is not sufficiently large to make a material difference in the outcome.

Another problem which has been difficult to evaluate has been that of mucocutaneous relapse and reinfection. At the New York Hospital my associates and I have tended to regard all cases in which *Spirochaeta pallida* reappeared at the site of the original lesion while there was any evidence of persistent reagin in the serum as cases of mucocutaneous relapse. Perhaps we have been too conservative.

What degree of success ought to be expected from such a method of treatment in order to render it practical? In 1932 Dr Stokes, in commenting on the Cooperative Clinical Group study of the results of the treatment of early syphilis by a variety of methods, said that the Wassermann reaction was found to be permanently reversed at six months in

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From the Syphilis Clinic of the Department of Medicine of Cornell University Medical College and the New York Hospital. The department was aided by grants from the Milbank Memorial Fund and the Barbara Henry Research Fund.

.71 per cent of cases. In this same series, there were cutaneous recurrences in approximately 11 per cent of the cases and serologic relapses in 14 per cent. Other authorities have estimated that 60 to 70 per cent of patients treated by a variety of methods throughout the country have a successful outcome. Any method of treatment capable of duplicating or improving on those results would seem worthy of consideration.

PATIENTS TREATED WITH NEOARSPHENAMINE

Forty-one patients treated by neoarsphenamine were referred to the New York Hospital for follow-up study.

Immediate Complications.

Icteric index over 15	5 cases
Peripheral neuritis (mild)	14
Peripheral neuritis (severe)	1
Dermatitis (mild)	2

All made rapid recoveries from these complications with the exception of 1 patient, in whom peripheral neuritis persisted for three months. Twenty-three patients (56 per cent) are still under observation and have had negative reactions of the blood and of the spinal fluid. One patient (2.4 per cent) recently died of carcinoma but was in the latter category.

In 14 cases (34.1 per cent) follow-up visits were allowed to lapse. Ten of the 14 patients (24.5 per cent) were seronegative or practically so when last seen.

I believe that one may justifiably include 34 of the 41 patients (82.9 per cent) in the group with successful results. The failures consisted of 3 patients (7.3 per cent) with infectious relapse and 4 patients (9.8 per cent) who dropped from observation while still seropositive, making a total of 17.1 per cent of failures or potential failures.

These figures correspond closely with those of the follow-up study, based on the whole series, reported by Dr. Baehr a year ago.

PATIENTS TREATED WITH MAPHARSEN

Dose of Less Than 1,200 Mg.—Of 73 patients, 9 (12.3 per cent) have had infectious relapses and 4 (5.5 per cent) have had serologic relapses. Thus 13, or approximately 18 per cent, have been unquestionable failures. In addition, 7 patients (9.6 per cent) were lost while still seropositive. Thus, 20 patients, or 27.4 per cent of the total, have had an unsatisfactory or potentially unsatisfactory outcome. Four (5.5 per cent) are still seropositive at six months and hence fall in an indeterminate group.

Forty-nine patients (67.1 per cent) are seronegative or nearly so now, or were when last seen

In summary, 27.4 per cent of this group have had an unsatisfactory outcome, either through failure of treatment or through lapse of follow-up visits while they were still seropositive, 67.1 per cent have had a successful termination, and in 5.5 per cent the outcome is still uncertain

Dose of 1,200 Mg—Since the first of the patients given this dose arrived at the hospital about Sept. 1, 1939, the period of observation has not been long enough to warrant any conclusions. Thirty-eight patients have reported to date. In this group, infectious relapses have occurred in 2 (5.3 per cent). Seven patients (18.4 per cent) have been followed for six months or more, and are all seronegative.

Complications—No serious complications of treatment were observed in the series of patients treated with mapharsen. There were some mild complications:

Icteric index over 15	12 cases
Peripheral neuritis (mild)	5 cases

All of the patients with these complications made rapid and uneventful recoveries.

CONCLUSIONS

In my experience, the results with neoarsphenamine were better than those with less than 1,200 mg. of mapharsen. What the outcome in the series receiving 1,200 mg. will be remains to be seen. It must be realized that no observations are yet available as to the remote outcome as far as the cardiovascular or central nervous system is concerned. However, at present it seems that this method of treatment compares favorably in regard to both immediate complications and results with standard methods of treatment as applied throughout the country.

From the point of view of the general adoption of this therapy, I feel strongly that as yet it should be limited to organizations or institutions in which adequate follow-up study is assured. The failures represent a public health menace which cannot be taken lightly.

In my opinion, this method of treatment represents a real advance in the chemotherapy of syphilis. Perhaps the eventual outcome will be a modification of this method. Such modifications should be aimed at a reduction of the serologic and cutaneous relapses. When this is accomplished, the result will be a practical, highly efficient method for use in the control of syphilis.

MASSIVE ARSENOTHERAPY IN EARLY SYPHILIS BY THE CONTINUOUS INTRAVENOUS DRIP METHOD

FOLLOW-UP OBSERVATIONS AT BELLEVUE HOSPITAL

EVAN THOMAS, M.D.

NEW YORK

The essential facts regarding the patients observed at Bellevue Hospital after treatment with the intravenous drip method of administering massive doses of arsenical compounds have already been presented. I have no change to make in them, and I think that there is no disagreement about the facts. The more I deal with statistics, the less confident I am that they always present satisfactory pictures of the facts, but they are obviously necessary evils. Thus opinions regarding relapsing infectious syphilitic lesions and reinfections may differ, but as long as the facts are presented one can make his own statistics. It seems to me that patients lost to observation belong to the unknown and should be left there. The variables in syphilis are difficult enough without this factor, but it is legitimate to point out statistically the percentage of known good results in the total number of patients treated. To do more than this with unknown factors is to bring deliberate speculation and doubt into statistical material which claims to be factual.

Of the 42 patients treated with neoarsphenamine and followed at Bellevue Hospital, 3 were lost from observation within six months. One of them had a negative Wassermann reaction of the blood before he disappeared. Fifteen, or 35.7 per cent, had definite peripheral polyneuritis, lasting as long as ten months in 1 case. In this series there were no other toxic symptoms observed. One hundred and twenty-two patients treated with mapharsen have reported to Bellevue Hospital. None of them presented any toxic manifestations under observation, with the possible exception of a man in whom jaundice developed six months after the treatment.

There seems to be no question that neoarsphenamine is a much more toxic drug than mapharsen, but it is an interesting fact that many of the patients in both series volunteered the information that they felt much better after the treatment than they had for a long time prior to it. Perhaps some of this can be attributed to rest and care in the hospital,

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but one cannot ignore entirely the possibility of a genuine tonic action by the drugs themselves. Two patients gave a history of rheumatic fever and had cardiac disease due to rheumatic fever. Four showed roentgenographic evidence of pulmonary tuberculosis. In one the condition was probably active at the time of treatment, and he was recently sent to a sanatorium by members of the chest service at the hospital. It was the opinion of these physicians, however, that antisyphilitic treatment had not caused any exacerbation of the pulmonary lesions.

In the neoarsphenamine series new genital lesions developed in 3 patients after treatment. Two of these seemed to me to have fairly clean-cut examples of reinfection. Both had negative Wassermann reactions of the blood at the time their new lesions appeared. Unfortunately spirochetes were not found in either case, although dark field examinations were made by several different persons and in 1 case at two different clinics. In both patients, however, secondary manifestations and positive serologic reactions appeared while they were under observation. One named the source of his probable reinfection, and the woman was placed under treatment. The third patient may have an infectious relapse. Three months after treatment a penile lesion developed in which dark field examination at the Charles V. Chapin Hospital in Providence, R. I., showed spirochetes, at the same time he had a plus-minus Wassermann reaction of the blood with the cholesterolized antigen only and a questionably positive result of a Hinton test. He received standard routine therapy for four months and returned to New York but failed to report to the clinic for another ten months, when relapsing lesions developed on the genitalia, material from which showed spirochetes on dark field examination. I have no knowledge of any blood tests performed during the interval between his routine therapy and relapse. All 3 patients were retreated with mapharsen, without difficulty.

In the mapharsen series 84 patients had less than 1.2 Gm. Nine were lost from observation and the treatment was a failure in 8, 7 of whom have been retreated. Of the 8 failures, 1 patient had relapsing lesions with spirochetes and 3 had possible infectious relapses, since they had sore throats which were moderately injected. Of the patients receiving 1,200 mg. of mapharsen, 1 with what seemed to be a clean-cut reinfection has been retreated. Thus in the entire series there were 3 probable reinfections, 2 infectious relapses according to dark field examination and 3 probable infectious relapses as judged by sore throats. In addition, 1 of the neoarsphenamine series and 3 of the mapharsen series remained seropositive, and there was 1 serologic relapse without clinical symptoms.

I have limited this report to toxicity and infectious relapse or reinfections because it seems that they are the two most important clinical

factors arising from the experiment. It may be of interest that in the past four years I have seen 5 deaths attributed to neoarsphenamine or arsphenamine in the course of routine therapy. Two of the patients were from the clinic in Bellevue hospital. One died of aplastic anemia, and in the other acute yellow atrophy developed in the course of arsenical hepatitis. Of the other 3 patients, the condition in 1 was diagnosed by the neurologist as hemorrhagic encephalitis, and the other 2 died of second attacks of exfoliative dermatitis. Of 1,021 patients with early syphilis admitted to the wards of Bellevue Hospital in the past four years, in 59, or 5.8 per cent, the condition was diagnosed as relapsing infectious syphilis and in 3 as possible reinfection. I have not reviewed all of their charts, but of the last 10 patients with a diagnosis of relapsing secondary syphilis, 7 had had their lesions for over four weeks and 1 had made five visits to a New York clinic before the diagnosis was made. Thus with neither type of treatment has the menace of infectious relapse been overcome, but the intensive form of therapy can scarcely be a greater hazard in this respect than present methods. Obviously patients treated by the intensive method must be followed at frequent intervals over a period of years and checked the rest of their lives, when this is possible; but I do not believe that this presents any greater problem than the present routine method of treatment.

MASSIVE ARSENOTHERAPY IN EARLY SYPHILIS BY THE INTRAVENOUS DRIP METHOD

ARSENIC EXCRETION IN THE URINE AND CONCENTRATION IN THE BLOOD

HARRY SOBOTKA, PH D

WALTER MANN, BS

AND

EDITH FELDBAU

NEW YORK

EXCRETION OF ARSENIC

In the course of the study of continuous intravenous drip therapy of early syphilis, we had the opportunity to study the excretion of arsenic in the feces and urine of 35 patients during the period of treatment in the hospital. A few years ago the urinary excretion of arsenic was studied in this laboratory after therapy with massive doses of neoarsphenamine in 24 patients¹. The patients had received 2.4 to 5 Gm, with an average of 4 Gm, of neoarsphenamine during the treatment, which lasted for four to six days. The amount of arsenic administered varied between 480 and 1,000 mg, of which 77 to 290 mg was found to be excreted in the urine. The percentage of elimination varied from 11.6 to 37.2 during the treatment period, usually of five days, with an average of 21.1 per cent.

Since a greater fraction of the arsenic is expected to be excreted through the intestinal tract than through the kidneys, a new series of studies was undertaken in which the analysis was extended to the feces.

Method—The arsenic was determined by an adaptation of the method of Morris and Calvery² to photoelectric colorimetry. The method consists of wet ashing with a mixture of nitric, sulfuric and perchloric acids. The digest is distilled, according to Marsh, using an aliquot portion after making up 100 cc. The gas current is scrubbed by passing through a layer of washed sea sand drenched

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1 Chargin, L., Leifer, W., and Hyman, H. T. Studies of Velocity and Response to Intravenous Injections. Application of Intravenous Drip Method to Chemotherapy as Illustrated by Massive Doses of Arsphenamine in Treatment of Early Syphilis, *J. A. M. A.* 104:878 (March 16) 1935.

2 Morris, H. J., and Calvery, H. O. The Determination of Arsenic in Small Amounts in Biologic Materials, *Indust. & Engin. Chem.* 9:447 (April) 1937.

with lead acetate solution. The arsenic mirror is then developed in a quartz tube heated in an electric microfurnace. The arsenic mirror is dissolved in 0.2 cc. of nitric acid. After driving off the nitric acid, the residue is taken up with 10 cc. of a solution of hydrazine sulfate and ammonium molybdate. This represents twice the amount of the reagent used by Morris and Calvery. The reagent is prepared as follows: Twenty parts of a 1 per cent solution of ammonium molybdate in five normal sulfuric acid and 2 parts of a 0.15 per cent solution of hydrazine sulfate are made up to 100 parts. The blue color developed on heating for ten minutes on the boiling water bath was measured in a photoelectric colorimeter (photometer of Central Scientific Company) using an orange filter (Cenco 4) absorbing all wavelengths below 567 millimicrons. A curve was constructed for a concentration range from 5 to 100 micrograms of arsenic and a layer of 10 mm. thickness with a diaphragm opening to render water = 100. When plotting the arsenic reading against the galvanometric reading, the latter on the logarithmic scale of semilogarithmic paper, a straight line is obtained.

TABLE 1.—*Urinary Excretion of Arsenic During Neoarsphenamine Therapy*

Case	Neoarsphen- amine, in Gm.	Arsenic, in Mg.	Per Cent Arsenic Excreted in Urine During Therapy (Five Days)	Per Cent Arsenic Unaccounted For
1.....	4.4	880	24.9	75.1
2.....	4.0	800	17.7	82.3
3.....	4.3	860	13.7	86.3
4.....	4.3	860	16.4	83.6
5.....	3.8	760	14.6	77.2
6.....	4.0	800	19.3	85.4
7.....	4.0	800	20.6	80.7
8.....	4.5	900	18.4	79.4
9.....	4.3	860	15.4	81.6
10.....	4.0	840	16.2	84.6
11.....	4.2	840	20.8	83.8
12.....	4.2	880	22.9	79.2
13.....	4.4	840	18.7	77.1
Average.....	4.2			81.3

Aliquot samples were used for the analysis of the daily urinary output. The feces for twenty-four hours were pooled and homogenized in a ball mill and aliquot samples taken for analysis.

Results.—Table 1 summarizes the data for 13 patients treated with neoarsphenamine for whom urines only were analyzed. The urinary excretion varied between 13.7 and 24.9 per cent, averaging 18.7 per cent, in excellent agreement with the results of the preceding series.

Table 2 contains the data for 12 patients likewise treated with neoarsphenamine for whom analyses were made of feces and urine. The excretion of arsenic by these patients during the five day period of therapy was 16.7 to 24.3 per cent, averaging 30.6 per cent, in the feces. The total excretion varied from 33.5 to 66.6 per cent, with an average of 50.4 per cent.

Since this left practically one half of the injected arsenic unaccounted for, we investigated the amount of arsenic excreted for a short period

after termination of the therapy, as we had observed that the excretion does not rise to maximum values until the second to fourth day after initiation of the treatment. The amount of arsenic excreted in the urine during post-therapy periods, averaging thirty-six hours, was insignificant when compared to the amount cleared during therapy. However, up to 17 per cent additional arsenic was found excreted in the feces forty-eight hours after termination of therapy, and as much as 13 per

TABLE 2—*Excretion of Arsenic During Neoarsphenamine Therapy*

Case	Neoarsphenamine, in Gm	Arsenic, in Mg	Per Cent Arsenic Excreted				Per Cent Arsenic Unaccounted For
			During Therapy (Five Days)		After Therapy (Two Days)		
			Urine	Stool	Urine	Stool	
1	4 0	800	18 5	29 7		8 7	43 0
2	4 0	800	16 7	30 0			53 3
3	4 0	800	20 3	37 2	1 5	13 6	27 3
4	4 2	840	18 0	38 2	1 1	7 3	35 4
5	4 2	840	18 1	15 4	1 4		65 1
6	4 0	800	23 4	28 6	2 7	6 5	38 8
7	4 0	800	20 2	21 0	2 2		56 6
8	4 2	840	21 5	20 2	2 7		55 5
9	4 0	800	24 3	42 3	1 9	3 2	28 4
10	4 0	800	19 6	46 4	1 0		33 0
11	4 2	840	19 4	28 4	1 3	15 1	35 7
12	4 0	800	17 4	30 2	1 6	12 4	38 5
Average	4 1	815	19 9	30 6	1 5	5 6	42 7

TABLE 3—*Excretion of Arsenic During Mapharsen Therapy*

Case	Maphar- sen, in Gm	Arsenic, in Mg	Per Cent Arsenic Excreted				Per Cent Arsenic Unac- counted For
			During Therapy (Five Days)		After Therapy (Two Days)		
			Urine	Stool	Urine	Stool	
1	0.60	174	23.7	49.2	2.4	12.8	11.8
2	0.60	174	29.6	24.4	2.5	31.2	12.2
3	0.70	203	28.6	53.5	3.5	15.1	
4	0.70	203	32.6	22.6	3.8	42.3	
5	0.63	183	24.8	65.2	2.2		8.0
6	0.70	203	28.3	73.5	2.5		
7	0.70	203	28.9	37.4	0.9	7.3	14.7
8	0.70	203	17.3	19.5	0.9	31.8	29.4
9	0.90	261	23.4	43.5		7.9	25.3
10	1.00	290	17.2	34.2	1.2		47.4
Average	0.72	210	25.4	42.3	2.0	14.8	14.9

cent during the first twenty-four hour post-therapy period. These figures still leave a considerable fraction of the total amount of arsenic unaccounted for. One may anticipate that an additional amount of perhaps 10 per cent may have been eliminated in the feces during the following days, leaving a deficit of one fourth to one third of the injected arsenic. Some of this is presumably eliminated through the perspiration and some deposited, for the most part, in hair, nails and bone.

Table 3 deals with 10 patients who received between 600 and 1,000 mg of mapharsen by continuous intravenous drip during five days. This product contains 29 per cent arsenic.

The excretion during the five day period studied fluctuated between 17.2 and 29.6 per cent in the urine and 19.5 to 73.5 per cent in the feces. The total excretion varied from 36.8 to 90 per cent. The averages were 25.4 per cent for the urine, 42.3 per cent for the feces and 67.7 per cent for the total, figures which exceed the arsenic excretion after the administration of neoarsphenamine by one fourth. The excretion during the post-therapy period was about as high in this series as in the neoarsphenamine series. The exceptionally high values in cases 4 and 8 are due to retention of feces during the last days of treatment. It appears from these data that a high percentage of the arsenic of mapharsen is excreted through urine and feces in the majority of the cases when the drug is administered in amounts below 1,000 mg. in five days.

The observation in case 10 may indicate that the excretion of arsenic in patients receiving more than 1,000 mg. of mapharsen may show values approaching those of neoarsphenamine. In other words, when larger doses of mapharsen are administered by the continuous intravenous drip technic there may be a somewhat greater lag in excretion than with smaller doses.

ARSENIC CONTENT IN BLOOD DURING AND AFTER CONTINUOUS INTRAVENOUS TREATMENT

During the progress of the clinical work it became desirable to study the arsenic level in the blood during and after the course of treatment. The arsenic content of the blood was therefore studied in 18 cases.

Method.—Specimens of blood of at least 10 cc. each were obtained two to four times a day. This blood was ashed with the mixture of nitric, sulfuric and perchloric acids referred to in the description of the method for determining excreted arsenic. The residue was made up to 25 cc., and two portions of 10 cc. each were used for analysis, corresponding to 4 cc. of serum. The blank value for a complete combination of all the reagents used was frequently redetermined, at least every time when the use of a new batch of one or the other reagents was begun. This blank amounted to 0.2, 0.3 or 0.4 micrograms per determination and was used as correction.

Results.—Applying this correction we found the specimens before treatment invariably free of arsenic. The arsenic rose to values of 10 to 24 micrograms³ per hundred cubic centimeters at the end of the first twelve hour period of treatment and to values of 10 to 30 micrograms on the second day. It dropped and reached values from 0 to 12 during

3. One microgram is one millionth of a gram; hence, 10 micrograms in 100 cc. signifies a concentration of 1 part arsenic in 10,000,000, and 40 micrograms in 100 cc. signifies 1 part arsenic in 2,500,000.

the first night and from 0 to 17 during the second night. From then on the values oscillated between 28 and 40 micrograms as maximum values for the evening specimens and between 16 and 35 micrograms as minimum values for the morning specimens.

In 9 cases the arsenic level in the blood was studied for two further days after treatment, it showed a gradual decrease, in concordance with the observations made during the studies on excretion.

The results are summarized in charts 1 and 2.

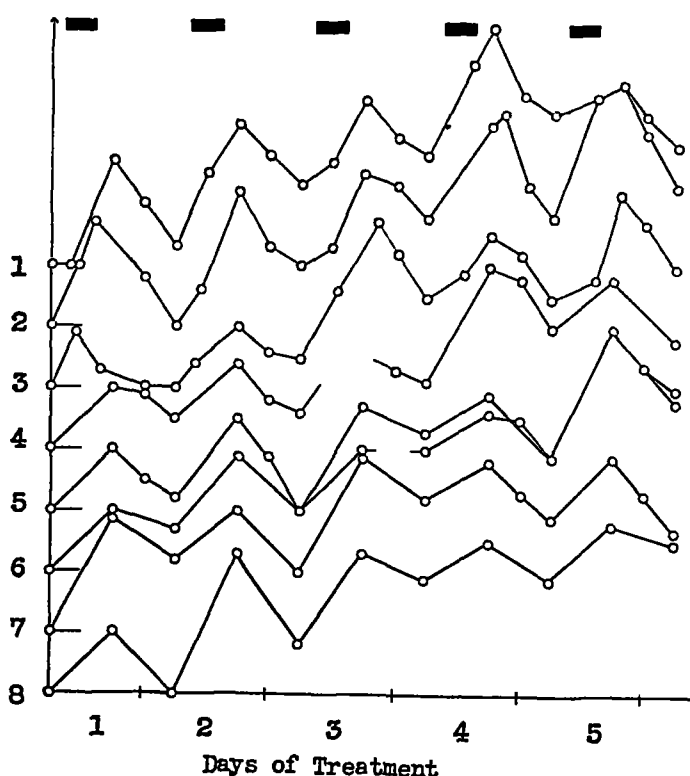


Chart 1—Arsenic level in the blood during intravenous treatment with arsenic. Eight cases were studied during five days of treatment. Each circle represents one double determination of arsenic, the first circle to the left, next to the case number, indicates the zero level for each individual graph. The zero level for each case is placed for convenience at an equal distance above the preceding one, and this distance corresponds to 10 micrograms of arsenic per hundred cubic centimeters. Hence, the initial value for case 7 signifies the 10 microgram line for case 8 and the initial value for 6 indicates the 10 microgram line for 7 as well as the 20 microgram line for case 8. The period of actual injection is indicated in black blocks.

Comment—Future studies of this nature in correlation with clinical and serologic follow-up observations may permit an evaluation of the significance of the behavior of the arsenic level of the blood on success and course of the cure. Of importance are probably the maximal con-

centrations in the blood obtained during treatment and the minimum values to which the arsenic drops during the intervals when treatment is discontinued. The sustained blood level during the later part of active treatment is comparable with the objective which has been considered important in other forms of chemotherapy.

The individual variations, in turn, indicate the individual ability to maintain the drug in the circulation and in the tissues. Furthermore, a study is desirable to determine the form in which the arsenic occurs

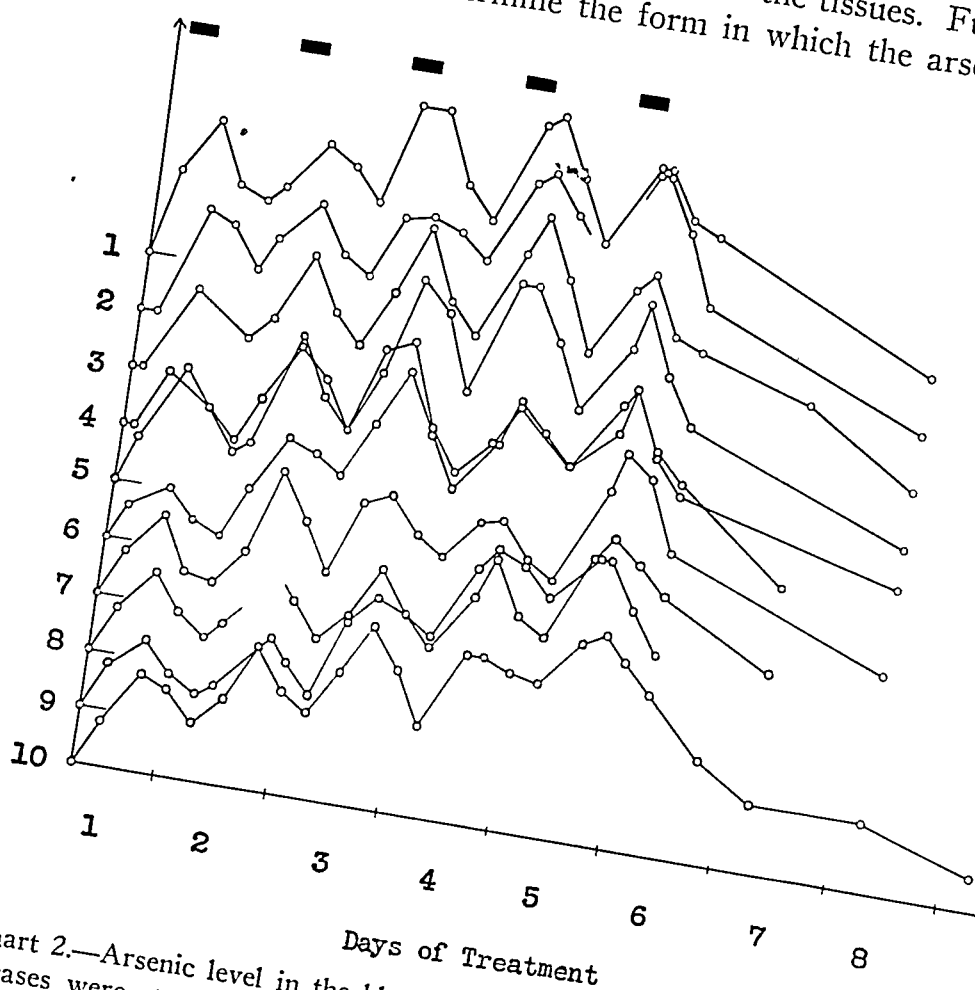


Chart 2.—Arsenic level in the blood during intravenous treatment with arsenic. Ten cases were studied during five days of therapy and several days thereafter. (See legend for chart 1.)

in the blood on the one hand and in the excreta on the other hand, especially with the new method of therapy. Finally, experimental studies on animals might throw light on the distribution of arsenicals in the various organs and tissues in comparison with the storage of arsenicals administered by single injection.

SUMMARY

The excretion of arsenic with the new intravenous drip method of arsenotherapy averaged 21 per cent of injected arsenic in the urine and

50 per cent in the combined excreta during the five days of treatment with 4 Gm of neoarsphenamine. Additional amounts were found excreted during an observation period of two or three days following treatment. On the administration of amounts up to 1 Gm of mapharsen by the intravenous drip method, the excretion averaged 67 per cent. The arsenic level in the blood showed a zigzag course with both minimum and maximum values rising during the first two days. On the third day and thereafter the blood level fluctuated between 16 and 40 micrograms per hundred cubic centimeters. The minimum values before the daily resumption of treatment were 16 to 35 micrograms per hundred cubic centimeters, whereas the daily rise brought them invariably above at least 28 micrograms.

DISCUSSION OF PAPERS BY DRS BAEHR, LEIFER, CHARGIN,
HYMAN, MAHONEY, WEBSTER, THOMAS, AND
SOBOTKA, MANN AND FELDBAU

DR C WALTER CLARKE, New York. My association with this project has been one of the most interesting and satisfactory experiences I can remember. I wish especially to compliment my colleagues on the excellence of their presentations of the facts.

I am sure that I speak for every member of the committee which controlled this highly significant demonstration of a new therapeutic method when I call attention to the limitation of the work. Our experience has been limited as to the type of syphilis treated, the type of treatment given and the duration of observation of treated patients.

It is worth while to emphasize the fact that we have treated only males with early syphilis. We do not know what the immediate results of our method would be in the treatment of latent syphilis, late syphilis, congenital syphilis, syphilis in pregnant women or even early syphilis in females. No assumptions should be made with regard to the treatment of these groups by the continuous intravenous drip method.

We have employed only neoarsphenamine and mapharsen. We have given five days of treatment in nearly all cases. We do not know what would be the effect of longer or shorter periods of treatment or of administering a bismuth compound or mercury before, during or after the arsenical treatment. All of this remains to be determined by further investigation.

Only a few patients have been followed for more than five years. The observations on this small group are most encouraging. Observations on the group followed for shorter periods of time are encouraging as to the immediate results. We cannot assume, however, that because the immediate results are so successful the permanent results will be equally brilliant. The immediate results, however, may justify the method, especially from the public health point of view, even though the permanent results are less impressive than we hope will prove to be true, for the immediate results will have an important effect on the spread of infection.

Perhaps a word of warning with regard to publicity is in order at this time. I think there is reason to fear that undue, sensational or inaccurate publicity may cause a great flood of applications to the Mount Sinai Hospital from victims of syphilis who are willing to sacrifice everything in order to take advantage of

what they will believe to be a marvelous new cure. Undue publicity would shake the confidence of thousands of syphilitic patients in the care which they are now receiving from their physicians. Many physicians would be placed in an awkward position when their patients demanded the five day cure which the doctors would not be prepared to administer.

It is well to point out that this method of treatment is not available, and probably will not become available for some time, to patients with syphilis throughout the country. There is danger also that a few physicians may undertake to administer treatment by the intravenous drip method with disastrous results to their patients. Such experiences may tend to discredit a method which in the hands of experts and in medical institutions of the highest quality gives great promise of success.

It seems to me that further carefully controlled scientific studies should be encouraged in as large a number of high grade medical centers as may be willing to undertake this work.

Finally, it is important to note that from a research point of view estimations of this method which do not provide for adequate and long continued follow-up of treated patients will be of little value, since it will not be possible to evaluate the permanent results.

DR. JOSEPH EARLE MOORE, Baltimore: I have already expressed myself in print (*The Massive Dose Arsenotherapy of Early Syphilis*, *Am. J. Syph., Gonorr. & Ven. Dis.* **23**:797 [Nov.] 1939) to the effect that I think this investigation may represent the most important advance in the treatment of syphilis since the original discovery of arsphenamine by Ehrlich in 1909. It is a familiar fact, of course, that since 1909 there has been going on in a number of chemotherapeutic laboratories throughout the world a search for new and better drugs to improve on arsphenamine, drugs which will act in less time, with more success and with less danger to the patient. Those efforts, although they have succeeded in producing a number of drugs which eliminate some of the technical difficulties and some of the minor dangers of treatment, have not yet been successful. No new drug has been shown to be therapeutically superior to old arsphenamine.

This experiment represents a new method of using existing drugs. The theory of the method is clearly based on an analogy to the effect of sulfanilamide in bacterial infections. The success of treatment of bacterial infections with sulfanilamide depends on a time-dose relation. Bacterial infections treated with sulfanilamide are not cured until the blood-tissue concentration of the drug is raised to a certain critical level. Moreover, if this critical level is not maintained for a sufficient period of time, there is a tendency to relapse.

With this particular method, time-dose relation is applied to the treatment of early syphilis, with interesting results. Nevertheless, in my opinion, much further study is essential before the method is ready for general clinical application.

The time-dose relation, i.e., the duration of treatment and the dose of the drug, whether neoarsphenamine or mapharsen, has apparently, as nearly as one can judge from published reports and from this presentation, been more or less arbitrarily chosen: five days of treatment and an arbitrary dosage which is determined largely on the basis of the patient's tolerance.

Perhaps this is not the first time-dose relation, and perhaps in the experimental laboratory something can be done to clarify the situation so that it may be possible to "cure" early syphilis in an even shorter time as successfully as this experiment has suggested that it may be "cured" in five days. Perhaps it may be possible to do it in five hours.

In the experimental laboratory, there are a number of things I should like to see done

1 Among these are toxicity determinations in animals with arsenicals given by this continuous intravenous method of drip administration. Data obtained by such studies do not at the moment exist. The minimal lethal dose and the maximal tolerated dose of the several arsenicals by this particular method are not known. Furthermore, it is essential to consider the question of the diluent used and the question of concomitant treatment. In an effort to prevent treatment reactions, the arsenical drugs used in this human experiment were administered in a 5 per cent solution of dextrose, and some patients were simultaneously given vitamin B₁ (thiamine chloride) and vitamin C. There are no adequate experimental data available as to the effect on toxicity or, even more important, on therapeutic efficiency of the arsenical drugs when given in this diluent or with concomitant vitamin therapy.

Animal experimentation to determine toxicity, moreover, should employ larger species than the rabbit. In rabbits immobilized on an animal board long enough to permit continuous intravenous drip, there are important alterations in body temperature. The administration of drugs during fever may significantly modify both toxicity and therapeutic efficiency. As yet no reliable data on these points are available.

2 I am interested, further, in the pathologic examination of animals killed at varying intervals of time after this form of treatment. What, if any, are the evidences of both immediate and remote damage to tissue? The fact that human beings may successfully tolerate this treatment without ill effects apparent within the next few months does not, to my mind, necessarily indicate that the treatment is harmless. Permanent ill effects may appear months or years afterward.

3 I should be interested in the concentration of the drug as such and of arsenic in blood and tissues. There is needed much elaboration of the work already begun on a small scale by the Mount Sinai group.

4 I am interested also in an accurate evaluation of the minimum effective dose for rabbits with syphilis by this means of treatment. These data, if and when available and when related to maximum tolerated dose by this method, may more accurately define the all-important time-dose relation.

5 Finally, I am interested in the relation of all these problems to the possible combination of fever therapy and chemotherapy. There are accumulating, gradually, both clinical and experimental data to indicate that a combination of fever therapy and chemotherapy for patients or laboratory animals with early syphilis may be more effective than either one alone. I am all for this type of investigation in the laboratory. There are many experiments that cannot be done on human beings which need urgently to be done before such a method as has been here described can, it seems to me, receive general application.

As to the clinical use of the method, many considerations influence its present availability for more general application. There are half a million freshly infected persons and no money to treat all of them by this expensive technic. This is a method which, because of its hospitalization requirement, is practically limited to urban areas and to only a few of those because of limited hospital space. In my hospital in Baltimore no beds are available, and I do not know where I could get any. Cost is an important factor which must be considered in relation to the cost of present methods.

The patient's loss of time needs further consideration. Dr. Rice suggested that hospitalization for early syphilis is desirable. In my opinion it is undesirable.

to take a patient with early syphilis away from his job and "out of circulation." It seems to me much better from the standpoint of his morale and of his economic situation for him to stay at work if he can.

The risk of the method, of course, is an all-important consideration. I am particularly impressed by the fact that, so far, in 374 patients treated there have been 4 examples of hemorrhagic encephalitis, of which 1 was fatal. The published and quoted data as to the incidence of hemorrhagic encephalitis with standard treatment methods are not accurate, at least so far as Baltimore is concerned. Among 30,000 patients with syphilis treated there, only 2 examples of hemorrhagic encephalitis have occurred. This is an incidence of 1 in 15,000 in place of an incidence of 1 in less than 100 here reported; and hemorrhagic encephalitis is one of the gravest complications of antisyphilitic treatment.

The therapeutic result of this method of treatment must, it seems to me, be measured not only against the results of the best form of standard treatment but also against the results of the poorest form. In other words, are the good results of the intravenous drip method superior to the results of one to three injections of an arsenical by the standard method? Not much is known about the results of poor standard treatment; but on the basis of a five to ten year follow-up of a large series of cases at the Johns Hopkins Hospital, they are about 65 per cent satisfactory. That is to say, 65 per cent of patients are "cured" both clinically and serologically by from only one to three standard injections of old arsphenamine. The results of massive arsenotherapy are perhaps 20 to 25 per cent better, but at an enormously increased cost to the community and increased risk to the patient.

Another point which occurs to me is whether one might accomplish the same result (and this too is best determined in the laboratory rather than in the clinic) by means of multiple divided doses instead of the continuous drip. May it not be possible to give the patient two, three, four or five divided doses within a given day or over a period of several days, with less inconvenience, equal safety and equally satisfactory results?

Finally, as Dr. Clarke has pointed out, I am, like many others, interested in the application of this method of treatment to late syphilis. Here is a different sort of problem. The question of infectiousness is not involved, but the treatment of late syphilis is a problem of even greater importance to the public health than that of early syphilis. There is four times as much late as early syphilis. In physical breakdown of the individual patient and in community expense, late syphilis is as urgent a public health problem as cancer.

It seems to me that the group of physicians at Mount Sinai Hospital, in originating this new thought in the treatment of syphilis, has bitten itself off a lifetime job, one which, as Dr. Vonderlehr has said, deserves the utmost help from all possible directions and with the utmost speed.

My own personal feeling is that much still remains to be done, however. It will, I think, be a number of years before results are available which justify the routine adoption of the system, and I think it ought not to be adopted in the meanwhile except as a research project.

DR. JOHN H. STOKES, Philadelphia: This study is certainly impressive. I have had disconcerting experiences in watching the prolonged disposition to relapses of patients who looked at the start as if they would have good results, especially when serologic reactions of the blood are the chief criteria; in some persons the serologic reactions reverse readily and stay negative for one, two or three years and then a dangerous relapse occurs. I think it is not altogether

settled yet where this method will stand with reference to the control of relapses in patients. Relapse in patients is an inevitability. The best methods produce a certain number of them.

Some emphasis has been placed on the question that with this method for a week the physician has the patient under control, whereas in a clinic there is no control over him, and he is in the clinic for an hour and then out for the rest of the week. I have watched the educational functions of the clinics as far as patients are concerned for a time, and I should say that one would have to weigh rather carefully the alleged period of repeated contacts of the patient with a clinic staff that is really setting out to educate him.

Most of the staffs, in the hurry and scramble of work, have no chance to educate the patient, and the result is a defective follow-up study, but the short time the syphilitic patient remains under observation is not wholly a disadvantage, and he can be educated to a knowledge of the disease and to feel a responsibility toward it. It is even apparent that the best contact tracing is not done in the first visit or in the first two visits of the patient to the clinic.

It requires intensive confessional effort while the patient is in bed receiving the drip to get him to tell the source of his infection, whereas after a visit or two, it appears his memory refreshes and he becomes interested in the problem and becomes better. I do not think one can afford to lose sight of the critical problem of tracing the source of the infection and the directions in which it has moved.

I hope that one direction in which the experiment will branch out will be the use of some additional treatment, perhaps on some other angle of approach. I cannot say what it might be or what direction it might take. The total of good results might be increased and the proportion of relapses might be materially lowered. I hope it will not be considered that the six days in the hospital ends the treatment as far as the further intelligent management of syphilitic patients is concerned. I hope to see an increase in the number of spinal fluids examined.

I think Dr. Mahoney's prediction on behalf of the serologic tests is interesting, as to what serology means with reference to cure. I am anxious to see whether any difference appears between seronegative and seropositive patients with primary syphilis.

I was impressed by what amounted almost to the statement that all seronegative patients with primary syphilis treated by this method promptly became seropositive. It furthers the concept of abortive cure, which I have thought has some weak spots in it.

DR. HAROLD N. COLE, Cleveland. Through the kindness of Dr. Leifer and Dr. Chargin, this morning I had the pleasure of seeing 6 or 8 patients treated in this manner. I was surprised to find out how simple the technic was. I marvel at Dr. Chargin's working out this scheme of therapy, using the plan suggested by Dr. Hyman, and certainly the approach is closer to Ehrlich's idea of handling cases of syphilis than any method used thus far.

In Cleveland the physicians have attempted to handle all the patients with acute syphilis that come to the City Hospital or to the University Hospitals in the beds that the city has, and I have been thinking of how much could be saved if this system were inaugurated there and this method of taking care of the patients with early syphilis could be employed.

I agree with Dr. Moore that this achievement is one of the greatest that has been made since the time of Ehrlich and that the future for it is tremendous.

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As to Dr. Clarke's remarks concerning publicity of the method, I think still another phase must be considered. I hope this is not going to lead to publicity that will get the young men to feel, "Well, syphilis five days—that is the end!"

DR. R. A. VONDERLEHR, Washington, D. C.: I had the privilege of discussing Dr. Hyman's paper before the American Medical Association last year. I was impressed by the clinical results which had been obtained during the relatively short period of observation. It is true that the observation period was short and one could not make a final decision on the basis of the meager figures; nevertheless, the results did look good even for the patients treated with neoarsphenamine. I was, however, definitely disturbed by the large percentage of untoward reactions to the treatment and especially, in the neoarsphenamine group, by the relatively high instance of polyneuritis. I believe serious polyneuritis occurred in 10 per cent of the patients.

I am greatly impressed with the clinical results after the use of mapharsen. I am not nearly as pessimistic as when the first results came out based entirely on the use of neoarsphenamine.

I think that this investigation must be carried forward, because from a social and economic standpoint and from every public health angle, it has the greatest possible importance. It seems to me that for the past thirty years a single shotgun in administering the arsphenamines has been used. But, thanks to this group of experimenters, it has been made possible to shoot Dr. Ehrlich's "magic bullet" in one of the more modern machine guns.

DR. E. R. GENTRY, Governors Island, N. Y.: I do not think I have anything to say that has not been brought out. If this work is begun in the military service, it will be possible to hospitalize all the patients and to carry their records forward for a number of years probably better than has been done by any other group in the country.

I am interested in what has been brought out here this afternoon, and I hope to see the work carried along further.

DR. C. S. STEVENSON: I came to this meeting not to speak on this most important advance in the management of syphilis but to listen and learn about the developments connected with the employment of a less toxic arsenical.

For the past twenty-five years each new admission to the navy's sick list with syphilis has averaged about sixteen sick days. If by the employment of this method this loss of manpower can be reduced by two thirds, the saving in time alone will be sufficient to keep two capital ships in commission.

The medical corps of the navy is watching with an interest amounting almost to impatience the development of this method to the point of acceptance as a recognized clinical procedure.

I agree that lay publicity concerning this treatment may be an unfortunate reality, but I hope the layman's intelligent interest in a practical approach to a national problem will stimulate a widened field of scientific investigation and thus shorten the time before this, or an improved, technic can be adopted by a large group of clinicians and thus greatly reduce the spread of syphilis.

DR. HUGH J. MORGAN, Nashville, Tenn.: I am impressed by the great importance of the work which has been presented this afternoon. It is important not only from the point of view of public health but from the point of view of the individual patient.

There is one point which has not been touched on. It seems that mucocutaneous relapses continue to be a problem of the same magnitude in massive

intravenous therapy as in conventional treatment, I wonder if it will not be found that relapses will occur less frequently in persons whose syphilis has passed into the so-called secondary stage before massive treatment is instituted than in those who are treated when the disease is in the seronegative primary stage. With conventional treatment mucocutaneous relapses are more common in the persons with seronegative primary syphilis. It appears that in the early stages treatment prevents the full development of immunity or resistance which is engendered by the experience of several weeks of active syphilitic infection.

DR B I KAPLAN, Ossining, N Y I am not yet able to say much about the work at Sing Sing prison. The method as described is employed in the treatment of latent syphilis and asymptomatic neurosyphilis. To date it has been used for about four months in the treatment of 70 patients, with no serious reactions.

At this time I am in no position to comment on the effectiveness of this type of therapy in the treatment of latent syphilis, there is still much to be done as far as dosage and vehicle are concerned.

DR E S GODFREY JR, Albany, N Y I am not a syphilologist, and yet I have been interested for a long time in this field. I do not feel as Dr Clarke does that this method ought to be kept closed to a small group in order that cases may be followed up over a period of years. Scientists always want to be sure of something before they let it out to the public or to the general practitioners. That is a natural reaction, and yet when they so delay, the amount of experimentation that is possible is severely limited. Eventually, this method will be thrown open to a great many more physicians if it proves to be all that it presently indicates in the treatment of syphilis. I think it has the greatest promise of any work in this field since Ehrlich's announcement of arsphenamine.

The real deficiency up to this time is experience with this method for women and for patients with latent or late syphilis.

On the other hand, Dr Stokes was not as explicit as he has been in times past about the deficiency of the ordinary physician in the treatment of syphilis. I do not think that it hurts anything to acknowledge that there is something with which the regular practitioner is not acquainted.

I do not think that this technic is for office practice, but I can remember the early days of arsphenamine treatment, when \$35 and more was charged for a treatment and all patients were hospitalized. Yet it was only through the application of arsphenamine by the general practitioner that a great many of the deficiencies of treatment with it were brought out. I do not think this therapy ought to have the kind of publicity that reaches the headlines, yet, on the other hand, it does seem to me the experiments ought to be carried out in many more hospitals and institutions than are represented at the present time. To that end, I think there ought to be a suitable description of this work for physicians who are capable of giving the treatment with reasonable safety, and the results should be judged on the basis of this wider experience with less expert supervision.

MASSIVE ARSENOTHERAPY IN EARLY SYPHILIS BY THE CONTINUOUS INTRAVENOUS DRIP METHOD

PUBLIC HEALTH ASPECTS

JOHN L. RICE, M.D.
NEW YORK

Massive arsenotherapy by continuous intravenous drip seems to offer new hope for the control of syphilis and merits significant consideration by public health officers as well as by clinicians. Taking a large proportion of them permanently noninfectious and even curing a number of them add to the health of the community immeasurably. Prevention of the spread of this epidemic disease is thereby assured. The advantages of this short period of treatment in the management of latent and late syphilis are as yet undetermined, but here of cost seem obvious. The effects of this type of treatment in the again the opportunity for improvement over present methods may indeed prove a boon.

The modern syphilis control program embodies elaborate and costly machinery for case finding and case holding. A great deal of this work will at one stroke be eliminated and made unnecessary by the ultimate perfection and universal application of this five or six day treatment with massive doses. When the fact is considered that even in well organized syphilis clinics the lapse rate is great—the cooperative clinic group reported that of 6,807 patients with early syphilis, 5,718 (84 per cent) had allowed treatment to lapse before receiving twenty injections of an arsenical drug—the actual and potential value of the massive dose rapid therapy looms up as a genuine advance.

It should be possible with the first course of treatment to render permanently noninfectious at least 80 per cent of those infected with early syphilis, and it is conceivable that this figure may be even higher. The second course of treatment would clear virtually all of the remaining persons whose serum for some reason beyond present knowledge continues to give positive reactions.

Read at a Conference on Massive Arsenotherapy in Early Syphilis by the Continuous Intravenous Drip Method at Mount Sinai Hospital, New York, April 12, 1940.

The development and practical application of such a program would undoubtedly result in a tremendous saving in dollars and cents, in human suffering and disability and in lives. Governor Lehman said recently that a patient with early syphilis can be treated for about \$100 at public expense, but that it costs the state \$730 a year to maintain a patient with late syphilis in one of its institutions. He mentioned a single victim of late syphilis on whom the state had spent more than \$20,000 for hospitalization.

At this time it is particularly important to stress the applicability of massive dose chemotherapy to syphilis control in military forces. It would also result in tremendous savings in the treatment of the migratory and transient groups which are an ever present problem in certain sections of this country and even in a great city such as New York.

The manner in which this research project was organized and administered is one which, I believe, deserves mention here today. The work described, which has been presented as a unified mass experiment, was made possible only through the collaboration of a number of official and voluntary agencies and was supported entirely by grants from philanthropic foundations. There was no connection with any commercial organization. A committee composed of representatives of the United States Public Health Service, the New York City Health Department, the American Social Hygiene Association, the heads of the departments of medicine at New York, Presbyterian and Mount Sinai hospitals and the head of the department of pharmacology of Columbia University assumed responsibility for the work and has guided the project with the greatest care in all of its phases. This work would not have been possible had it not been for the painstaking and scrupulous attention of the members of the committee.

EFFECT OF OINTMENT BASES ON THE SKIN

I. RESULTS OF PATCH TESTS WITH COMMONLY USED OINTMENT BASES

LEON F. RAY, M.D.
PORTLAND, ORE.

AND

IRVIN H. BLANK, Ph.D.
BOSTON

Complaints of discomfort or of extension of a dermatitis not infrequently follow the application of a bland preparation, such as petrolatum or boric acid ointment. It is frequently difficult to explain this reaction. Is it a mere coincidence; i. e., has the patient been exposed to some other irritating agent? Is the ointment an allergen? Is it a primary irritant? If the last is true, does the irritating action result from the chemical or physical properties of the ointment or from some combination of properties? Is the ointment base or one of the materials added to the base responsible for the irritation? In an attempt to answer some of these questions, a series of patch tests has been performed with many of the commonly used ointment bases, the compositions of which have been fairly well defined. It is hoped that future work will be concerned with the physical action of these materials on the skin.

Probably the most extensively used ointment base is petrolatum U. S. P. Petrolatum is not a single chemical compound, and the United States Pharmacopeia's specifications permit its chemical composition and physical properties to vary over wide limits. Aliphatic or aromatic hydrocarbons may be present; the molecular weights of the constituents may range from 500 to 1,000; the amount of unsaturated hydrocarbons may be little or as great as 10 per cent. In the tenth revision of the United States Pharmacopeia, petrolatum is used in making boric acid ointment; in the eleventh revision, white petrolatum is used. Seldom have irritations been reported which could be traced directly to petrolatum. The saturated hydrocarbons are stable compounds;¹ only the

From the Department of Dermatology and Syphilology, Harvard Medical School and the Massachusetts General Hospital, C. Guy Lane, M.D., Chief.
1. (a) White, R. P.: *The Dermatogoses or Occupational Affections of the Skin*, ed. 4, London, H. K. Lewis & Co., Ltd., 1934, p. 197. (b) Weber, L. F.: *External Causes of Dermatitis: A List of Irritants*, Arch. Dermat. & Syph. 35: 129 (Jan.) 1937.

unsaturated hydrocarbons may be expected to be sufficiently reactive to cause chemical irritation

Nine samples of petrolatum, samples A to I,² were obtained, the physical characteristics of which are shown in table 1. All complied with the United States Pharmacopeia's specifications. It may be stated that the average molecular weight for the hydrocarbons of sample F was greater than for any of the other samples, sample G had the lowest average molecular weight. Samples H and I contained the highest percentage of unsaturated hydrocarbons. Small amounts of each of these petrolatums were placed on pieces of white cotton flannel, which were subsequently put on the skin, covered with cellophane (not moisture proof) and held in place with adhesive tape. In all cases the materials were applied to the upper part of the back on normal-appearing skin for three days. Readings were made one to three hours after removal.

TABLE 1—*Specifications of the Petrolatums*

Petrolatum	Saybolt Melting Point	ASTM Consistency	Saybolt Viscosity at 210 F	Flash Point
A	110 120 F	185 220	58 63	420-430 F
B	110 120 F	180 220	61 66	420 430 F
C	110 120 F	175 220	62 67	420 430 F
D	112 122 F	170 220	65 70	420-430 F
E	112 122 F	170 220	65 75	420-430 F
F	120 130 F	185 220	45 50	360 370 F
G	110 120 F	185 220	55 60	410-420 F
H	105 112 F	210 240	50 55	360 370 F
I	105 112 F	215 255	50 55	360 370 F

Of the 79 patients studied, 24 had contact dermatitis, 10 had atopic dermatitis, 6 had various generalized dermatoses and the rest had such diseases as chancroid, dermatophytosis, syphilis, arsphenamine jaundice, pyogenic ulcers, lymphogranuloma venereum, lupus erythematosus, sarcoid, erythema induratum, lupus vulgaris, carcinoma and urticaria. These patients received a total of 559 tests with the petrolatum shown in table 1. Only two tests gave positive reactions, one an erythema and the other a papule. Both of these patients were subsequently tested by applying liberal quantities of the suspected base to the upper extremities and back for seventy-two hours. No detectable cutaneous reaction occurred, and it was felt that the positive reactions had been false.

If further tests are carried out on a large number of persons, some may be found who show a sensitivity or irritability to some or all of the petrolatums, as in the case reported by Hollander.³ Our data

2 These samples and their specifications were obtained from L. Sonneborn & Sons, Inc., New York.

3 Hollander L. Dermatitis Produced by Petrolatum. Report of a Case, *Arch Dermat & Syph* 38:49 (July) 1938.

indicate, however, that there are relatively few who are allergic to or chemically irritated by the petrolatums. No irritations to the petrolatums were obtained in this study, even though several petrolatums were used which were definitely known to vary in the molecular weight of their constituents and in the amount of unsaturated hydrocarbons present.

In addition to the petrolatums, the following materials which contain principally petrolatum were used for patch testing on each of the aforementioned 79 persons: ointment U. S. P., a special petrolatum base⁴ and a petrolatum base containing cholesterol esters. The results were uniformly negative.

Glycerite of starch, theobroma oil, benzoinated lard (all U. S. P.), glyceryl monostearate, cholesterol (Eastman organic chemical) and a cholesterol product containing a relatively high percentage of oxycholesterol produced no positive reactions to patch tests in any of the 79 persons studied.

The final group of compounds studied included hydrous wool fat and hydrous wool fat emollients. The specifications⁵ for the hydrous wool fat follow:

Melting point	38-42 C.
Moisture (maximum)	0.50%
Free fatty acid (as oleic).....	0.28%
Saponification number	85-110
Iodine value	18-36

The three emollients had the following composition:

	Gm. or Cc.
I. Stearic acid	21.0
Sodium borate	1.2
Potassium carbonate	0.4
Hydrous wool fat	90.3
Liquid petrolatum, heavy	22.5
Distilled water	122.6
Perfume	0.3
II. Stearic acid	56.0
Oleic acid	42.0
Hydrous wool fat	280.0
Triethanolamine	56.0
Distilled water	364.0
Perfume	1.2
Phenol	80.0
III. Same as (2) with phenol omitted.	

The results of the patch tests with these four materials are seen in table 2. It is interesting to note the large number of positive reactions

4. Formula for special petrolatum base: liquid petrolatum 30.5 cc., petrolatum 53 Gm., paraffin 16 Gm. and yellow wax 0.5 Gm.

5. Sample and specifications furnished by N. I. Malmstrom & Co., Brooklyn, N. Y.

obtained with emollients II and III as compared with I. Since I elicited only a few positive reactions to patch tests, and wool fat none, the hydrous wool fat was probably not responsible for the large number of positive reactions for II and III. Since all three emollients contained the same perfume, this was probably not the irritant. Preparations II and III varied from I in that they contained triethanolamine and oleic acid. Oleic and stearic acids have been shown to be relatively non-irritating.⁶ Goodman⁷ stated "Triethanolamine produces no irritations to the skin even if constituting as much as 15 per cent of the preparations."

TABLE 2—*Patch Tests with Hydrous Wool Fat and Hydrous Wool Fat Emollients*

	Negative	Erythema	Papule	Total	Per Cent Positive
Hydrous wool fat	75	0	0	75	00.0
Emollient I	71	4	4	79	10.1
Emollient II	23	30	14	67	65.7
Emollient III	22	29	6	57	61.4

Some time ago we had the opportunity of performing patch tests on nearly 100 nurses who had no apparent cutaneous lesions with four pure

TABLE 3—*Patch Tests with Triethanolamine Soaps*

	Negative	Erythema	Papule	Total	Per Cent Positive
Triethanolamine myristate	15	61	0	76	80.2
Triethanolamine palmitate	30	64	5	99	69.6
Triethanolamine stearate	48	44	3	95	49.4
Triethanolamine oleate	15	80	4	99	83.8

triethanolamine soaps. The test materials were applied to the skin for twenty-four hours only. The results of these tests, as shown in table 3, led us to believe that the presence in emollients II and III of triethanolamine, oleic acid and stearic acid, with the probable formation of triethanolamine soaps, was responsible for the large number of positive reactions seen with these materials. Irritations following the clinical use of preparations II and III were frequently observed.

SUMMARY

Nine petrolatums, all conforming to specifications of the United States Pharmacopeia but varying in molecular weight and in per-

6 Blank, I. H. Action of Soap on Skin, Arch. Dermat. & Syph. **39**: 811 (May) 1939.

7 Goodman, H. Cosmetic Dermatology. I. Triethanolamine, Arch. Dermat. & Syph. **36**: 116 (July) 1937.

centage of unsaturated hydrocarbons, consistently elicited negative reactions in patch tests on a group of 79 persons.

Patch tests with miscellaneous products, including ointment U. S. P., a special petrolatum base, a petrolatum base containing cholesterol esters, glycerite of starch, theobroma oil, benzoinated lard, glyceryl monostearate, wool fat, cholesterol and a cholesterol product containing a relatively high percentage of oxycholesterol likewise gave negative reactions.

Patch tests with hydrous wool fat and one emollient also gave few positive reactions. Two other hydrous wool fat emollients, however, gave a large number of positive reactions. These two emollients contained triethanolamine and fatty acids, and it is suggested that the irritating action of these emollients may be due to the presence of triethanolamine soaps, which were shown in another series of patch tests to give a high percentage of positive reactions to patch tests.

EXPERIMENTS IN POISON IVY SENSITIVITY

EFFECTS OF SPECIFIC INJECTIONS ON THE LEVEL OF SENSITIVITY
TO QUANTITATIVE PATCH TESTS AND ON CLINICAL SUSCEPTIBILITY

SOLOMON GREENBERG, M D

AND

ELLA D MALLOZZI, B S

NEW YORK

Since the introduction of specific immunologic measures for the treatment or prevention of poison ivy dermatitis, the more than one hundred year old controversy as to their usefulness has continued, and no decisive answer is at hand even today

It appears that desensitization was first suggested by the American Indian practice of chewing the leaves of the poison ivy plant Dakin,¹ in 1829, was probably the first medical authority to report the beneficial effects of specific desensitization He stated that laborers and other persons chewed the leaves to gain immunity and that physicians advised that the forbidden fruit be eaten

Alumbaugh,² in 1898, half filled a vial with the buds or leaves of *Rhus toxicodendron*, poured into the flask enough alcohol or whisky to fill it completely and allowed this to stand for one day He then made a third decimal dilution Twenty drops of this were placed in a glass of water One teaspoonful of the latter taken every hour cured, he said, in twenty-four to forty-eight hours

In 1902 Williams³ recommended that a decoction of the leaves be taken or that the leaves be chewed and their juice swallowed Ford,⁴ in 1907, thought that he had immunized rabbits and guinea pigs by subcutaneous injection, so that they resisted four to six times the original fatal dose and so that their serum protected other animals against the

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital

Dr Marion B Sulzberger gave valuable assistance

1 Dakin, R Remarks on a Cutaneous Affection Produced by Certain Poisonous Vegetables, *Am J M Sc* **4** 98-100, 1829

2 Alumbaugh, W E The Toxic Element of Poison Ivy, *Med World* **16** 298, 1898

3 Williams, T W Remedy for Poison Oak, *Med World* **20** 482, 1902

4 Ford, W W (a) Antibodies to Glucosides, with Special Reference to *Rhus Toxicodendron*, *J Infect Dis* **4** 541-551, 1907, (b) Artificial Immunity to Glucosides, *Science* **27** 652, 1908, (c) Note on *Rhus Toxicodendron*, *New York M J* **90** 215, 1909

fatal dose; however, on subsequent attempts he could not repeat his results. In 1913 von Adelung⁵ showed that the excitant is not fatal for rabbits and guinea pigs.

In 1918 Strickler⁶ stated his belief that it was possible to desensitize by intramuscular administration of the excitant, even though serums studied by means of complement fixation had proved negative. He said the immunity was a tissue immunity, evanescent, and one that had to be frequently renewed.

In 1919 Schamberg,⁷ returning to the oldest method, claimed to have desensitized human beings by feeding the tincture of *Rhus toxicodendron* in ascending doses throughout the poison ivy season, with uniformly successful results. Successful results with intramuscular injections of an alcoholic extract were then reported by Strickler⁸: 30 cases with no failures in 1921 and 95 per cent successful results in 1923. In 1923 Corson,⁹ following Strickler's method as to dosage and intervals, reported disappointing results. Good results were again reported, this time with the use of the combined method (injection and giving the tincture by mouth), by Williams,¹⁰ Bivings¹¹ and Williams and McGregor¹² in 1924 and by Alderson¹³ in 1925. In 1925, however, Krause and Weidman¹⁴ stated emphatically that the preventive treatment did not prevent the reaction and that the curative value was likewise scant or nil.

5. von Adelung, E.: An Experimental Study of Poison Oak, *Arch. Int. Med.* **11**:148-164 (Feb.) 1913.

6. Strickler, A.: Treatment of Dermatitis Venenata, *J. Cutan. Dis.* **36**:327 (June) 1918.

7. Schamberg, J. F.: Desensitization of Persons Against Poison Ivy, *J. A. M. A.* **73**:1213 (Oct. 18) 1919.

8. Strickler, A.: (a) Toxin Treatment of Dermatitis Venenata, *J. A. M. A.* **77**:910 (Sept. 17) 1921; (b) Toxin (Antigen) of *Rhus Toxicodendron* and *Rhus Venenata* in Treatment and Desensitization of Patients with Dermatitis Venenata, *ibid.* **80**:1588 (June 2) 1923.

9. Corson, E. F.: The Value of the Toxin of *Rhus Toxicodendron* and *Rhus Venenata*, *J. A. M. A.* **81**:59 (July 7) 1923.

10. Williams, C. F.: Ivy Poisoning, *M. J. & Rec. (supp.)* **119**:131 (June 4) 1924.

11. Bivings, G. L.: Successful Desensitization and Treatment of Poison Ivy and Poison Oak Poisoning, *Arch. Dermat. & Syph.* **9**:602 (May) 1924.

12. Williams, C. M., and McGregor, J. A.: Treatment of Ivy Poisoning by *Rhus* Tincture and Antigen, *Arch. Dermat. & Syph.* **10**:515 (Oct.) 1924.

13. Alderson, H. E.: Treatment of Poison Oak Dermatitis, *California & West. Med.* **23**:982 (Aug.) 1925.

14. Krause, G. L., and Weidman, F. D.: Ivy Poisoning: Preventive Treatment with Especial Reference to Individual Susceptibility, *J. A. M. A.* **84**:1996 (June 27) 1925.

A change in technic came about in 1925, when Clock¹⁵ substituted almond oil as the vehicle for the injection of the extract in place of alcohol, which had heretofore been used. This diminished the pain, which is a disagreeable effect of the injection of alcohol, and allowed a larger dose of the active principle to be given, since the oil is absorbed more slowly from the tissues. Clock and Gowen,¹⁶ in 1933, using this method, reported good results.

In 1936 Molitch and Poliakoff,¹⁷ giving the extracts by injection, reported excellent prophylactic results in a series of carefully controlled cases, in which one group received the extract and one group did not. Poison ivy dermatitis did not develop in the former group during the season, but it did in two thirds of the latter group. At the end of the season, 6 of each group were given poison ivy leaves to hold, and in 5 of the 6 in each group a dermatitis developed. The authors stated that this last form of exposure was evidently too stringent a test and concluded that the protection afforded was a matter of degree and was eminently satisfactory, provided the exposure was not excessive. Blank and Coca,¹⁸ also in 1936, found the extract to be extremely effective in preventing dermatitis from moderate exposures, the efficacy increasing with the quantity of extract given.

This short outline of some of the conflicting opinions serves to emphasize the divergence in the results obtained and to illustrate the often diametrically opposed views held by unquestionable authorities.

Such was the status of the problem when the present studies were commenced, in the spring of 1936.

Since the completion of our investigation (October 1936), several articles worthy of particular mention have appeared. The first is that of Molitch and Poliakoff.¹⁹ In 1937 they again reported a series of 50 cases, in the 42 patients who were given weekly injections (number not stated) of an alcoholic extract from the middle of the poison ivy season, not a single example of rhus dermatitis developed from the time of beginning the injections, in every one of the 8 who were left as controls and to whom no injections were given an eruption developed.

15 Clock, R. O. Rhus Dermatitis. Its Treatment with Poison Ivy Extract, *M. J. & Rec. (supp.)* **122** 93 (July 15) 1925, *Ann. Clin. Med.* **4** 519 (Jan.) 1926.

16 Gowen, G. H. Treatment and Prevention of Rhus Toxicodendron Poisoning, *J. Allergy* **4** 519 (Sept.) 1933. Clock¹⁵.

17 Molitch, M., and Poliakoff, S. Prevention of Dermatitis Venenata Due to Poison Ivy in Children, *Arch. Dermat. & Syph.* **33** 725 (April) 1936.

18 Blank, J. M., and Coca, A. F. Studies of Prophylactic Action of Extract of Poison Ivy in Control of Rhus Dermatitis, *J. Allergy* **7** 552 (Sept.) 1936.

19 Molitch, M., and Poliakoff, S. Prevention of Dermatitis Venenata Due to Poison Ivy in Children. Further Report, *Arch. Dermat. & Syph.* **36** 1086 (Nov.) 1937.

The second article is that of Simon and Lotspeich.²⁰ These investigators performed patch tests on 8 sensitive patients with three different dilutions of poison ivy extract (1:100, 1:1000 and 1:10,000). The subjects were then given a series of intramuscular injections of the specific extract and were subsequently retested with the aforementioned dilutions. The authors were able to demonstrate that the specific sensitivity of the skin was not appreciably altered, at least in so far as its capacity to react to the cutaneous tests was concerned.

The third study to be mentioned here is that of Zisserman and Birch.²¹ They studied a group of 1,731 boys at a Boy Scout camp on an island near Philadelphia. Three hundred and four boys received prophylactic intramuscular injections of the specific excitant. The incidence of subsequent poison ivy dermatitis in this treated group was 51.6 per cent, while the total incidence in the camp was only 33.6 per cent. The authors therefore concluded that the injections increased rather than decreased the clinical susceptibility to poison ivy dermatitis.²²

EXPERIMENTAL STUDIES

It was our opinion that the natural clinical exposures to poison ivy are often so variable, and their frequency, degree and manner so difficult to ascertain, that it is generally not advisable to judge the efficacy of prophylactic injections solely on the basis of subsequent clinical freedom from dermatitis. There are, moreover, many possible sources for error in evaluating the effectiveness of prophylactic measures in terms of clinical incidence of dermatitis. In this connection we may mention as an example the well known fact that after a severe attack it is not uncommon to observe a variable period of refractoriness to contact type dermatitis.

The problem of the efficacy of specific immunologic measures in the treatment and prophylaxis of eczematous dermatitis is of great importance, not only in relation to poison ivy and other plant dermatitis but also because of its bearing on the possible specific treatment and prophylaxis of contact type dermatitis in general.

For these reasons it was decided (1) to attempt experimental studies with the application of an objective, quantitative measure for determining

20. Simon, F. A., and Lotspeich, E.: Observations on Sensitivity to Poison Ivy, *J. Invest. Dermat.* **2**:143 (June) 1939.

21. Zisserman, L., and Birch, L.: The Prophylaxis and Treatment of Poison Ivy Dermatitis with an Extract of *Rhus Toxicodendron*, *J. Allergy* **10**:596 (Sept.) 1939.

22. The present experimental studies deal with problems of specific prophylaxis and not with specific treatment. We have therefore reviewed only the important previous studies on specific immunologic measures for prevention and have not included those on the specific treatment.

the degree of cutaneous sensitivity both before and after the administration of specific injections and (2) to attempt to determine the effect of specific injections on the clinical susceptibility to poison ivy dermatitis in a specifically treated group, as compared with a control group subjected to approximately equivalent natural exposures

Experiment 1—The study was carried out at two Civilian Conservation Corps camps in New Jersey on 382 adult men. The men were all engaged in work consisting mainly of clearing and building in areas in which there was a moderately but not unusually heavy growth of poison ivy.

The extract used throughout this experiment, as well as in all subsequent experiments, was prepared and supplied by a pharmaceutical company.²³

The method of extraction was as follows: poison ivy leaves were placed in acetone (preferably within four hours of gathering) for one month or more, treated with anhydrous calcium chloride and charcoal to remove the water and chlorophyll, and then boiled under vacuum to a concentration of 13 per cent solids. This material was added to sterile almond oil with 0.5 per cent chlorobutanol, in a proportion of 50 cc of the extract to 950 cc of the diluent. The solution was passed through a Berkefeld filter and then placed in ampules.²⁴

Each of the 382 men was given a patch test on the back and in the orthodox manner, with ten patches at the same time. Nine patch tests were made with the full strength extract and eight dilutions in acetone, 1:10, 1:100, 1:500, 1:1,000, 1:5,000, 1:10,000, 1:50,000 and 1:100,000. The tenth patch test was with a control solution of acetone in almond oil. In this way the level of sensitivity, i.e., the end point of reaction of each person at the particular time, was determined as accurately as possible. The readings of the responses elicited were graded 1 plus to 4 plus, depending on the amount and intensity of the erythema, vesiculation and edema.

Of the 382 men thus tested, only 278 could be closely observed during the entire six weeks of the experiment and only these are considered in the results here reported. Of the 278, 159 had no reactions whatsoever to the patch tests. These nonreactors received no injections but were merely observed in order to determine the incidence of ivy dermatitis in a group of exposed persons not reacting to cutaneous tests (experiments 3 and 4). The remaining 119 persons, i.e., all those who reacted to one or more patch tests with ivy extract, were arbitrarily

²³ Lederle Laboratories, Inc., Pearl River, N. Y.

²⁴ It is this material in the ampules which is referred to throughout this article as the full strength, concentrated or undiluted extract.

divided into two groups. The first group, comprising 77 subjects, received two intramuscular injections of the undiluted poison ivy extract in oil. A first injection of 1 cc. was given, followed in two weeks by a second injection of the same amount. The second group, which comprised the remaining 42 subjects who had reacted to patch tests, received two intramuscular injections of the blank vehicle (10 per cent acetone in almond oil), in doses of 1 cc. each, at intervals of two weeks.

TABLE 1.—*Comparison of Results of the First and of the Second Series of Serial Quantitative Patch Tests in Reactors Who Received Either Specific or Control Injections*

	Num- ber of Sub- jects	Sensitivity Unchanged After Injections		Sensitivity Greater After Injections		Sensitivity Less After Injections		Sensitivity Negative After Injections*	
		Num- ber	Per Cent	Num- ber	Per Cent	Num- ber	Per Cent	Num- ber	Per Cent
Received specific injections	77	34	44.0	23	30.0	20	26.0	12	15.0
Received control injections	42	12	28.5	12	28.5	18	43.0	12	28.5

* Included in the group under the heading "Sensitivity Less After Injections."

TABLE 2.—*Comparison of Strength of Solution Injected with the Reactions Obtained in Two Series of Experiments*

Strength of Solution	Reactions After Injections of Extract		Reactions After Control Injections	
	First Series	Second Series	First Series	Second Series
Full strength.....	36	21	29	13
1:10.....	23	16	8	7
1:100.....	12	13	5	6
1:500.....	0	10	0	3
1:1,000.....	1	2	0	1
1:5,000.....	0	3	0	0
1:10,000.....	0	0	0	0
1:50,000.....	0	0	0	0
1:100,000.....	0	0	0	0
Negative*.....	0	12	0	12

* At the time the patch tests were made there was no poison ivy eruption in any of the persons tested.

Six weeks after the injections were completed, the skin of all 159 subjects was again subjected to patch tests with the same quantitative serial dilutions of specific extract as had been employed in the first testing. The results of the comparison of changes in the levels of sensitivity to quantitative patch tests in the group treated with specific excitant and in the control group are set forth in table 1.

In table 2 we have listed for comparative purposes the dilutions of the extract used which elicited reactions in the first and in the second series of patch tests in persons who gave positive reactions after receiving either specific or control injections.

It is of interest at this point (table 3) to record the qualitative response to the full strength extract in the first series of patch tests of the subjects who gave "negative" reactions to the patch tests in the second series and in the subjects who received either specific or control injections

Under the conditions of experimentation and with the use of two intramuscular injections of the particular specific extract, no significant reduction of the skin's sensitivity to poison ivy could be objectively demonstrated by means of repeated quantitative patch tests on treated subjects and on a control group. There was, however, a decided fluctuation in the degree of sensitivity of many persons in both the specifically treated group and the control group, some increasing in sensitivity, some remaining unchanged and some decreasing in sensitivity. The phenomenon of decrease in sensitivity was more common among those

TABLE 3—*Comparison of Responses in Two Series of Patch Tests with Full Strength Extract After Injections of Extract or Control Solution*

Received injections of extract (full strength)	Number of Subjects 1*	First Series, Reading 3 plus	Second Series, Reading Negative
	2	2 plus	Negative
	3	1 plus	Negative
	6	Plus minus	Negative
Received control injections	1	2 plus	Negative
	4†	1 plus	Negative
	7	Plus minus	Negative

* An eruption of poison ivy developed between the two series
† An eruption of poison ivy developed between the two series in 1 person

receiving the control solution (43 per cent with decreased sensitivity, as compared with only 26 per cent in the extract group). We believe that in view of the fluctuations and the relatively small total numbers involved, it would be unwise to draw any conclusions from this figure at present. The last remark also applies to the finding that only 15 per cent of those receiving the extract gave entirely negative reactions to the second tests, while 28.5 per cent of those receiving the control solution demonstrated a change to complete lack of response.

Experiment 2—This experiment was designed to ascertain whether the specific injections as administered (experiment 1) reduced the incidence of clinical poison ivy sensitivity under the particular conditions of natural exposure obtaining during the experiment.

We included here a first group of 77 persons who had reacted to one or more patch tests and who received specific injections and a second group of 42 persons who had reacted to patch tests but who received only the control injections. Except for this one difference, these two groups were handled in exactly the same manner. All the men in both

groups were taught to recognize the plant and were told to use ordinary precautions to avoid exposure as much as possible. No extraordinary measures were used; i.e., no gloves or masks were worn, and no protective greases or other devices were employed. It may be said that while these men certainly did not "roll in the plants," their exposure was to be regarded as a natural, moderate to massive one and was probably roughly equivalent to that of children camping in a region in which poison ivy grows in average abundance. It is to be emphasized once again that, as nearly as it was possible to achieve this result, the exposures in the two groups were of roughly equivalent degree and nature. In addition to the numerical data set forth in the table it is to be mentioned that the average severity of the dermatitis was approximately equal in the two groups.

TABLE 4.—Comparison of Incidence of Poison Ivy Dermatitis in Patch Test Reactors Receiving Specific Injections with That in Patch Test Reactors Receiving Control Injections

Subjects	Number	Clinical Ivy Dermatitis Developed Within Six Weeks of Last Injection	
		Number	Per Cent
Subjects who had reacted to patch tests and had received specific injections	77	21	27
Subjects who had reacted to patch tests and had received control injections	42	15	36

Comment on Experiments 1 and 2.—In comparing results in the specifically treated group with those in the control group, it becomes apparent that the sensitivity as demonstrable by quantitative patch tests was apparently slightly increased after the specific injections, while the sensitivity as judged by the supervision of clinical dermatitis was decreased rather than increased after the specific treatment.

This, of course, brings up the question of the results of patch tests as an index of clinical sensitivity. It is to be remembered that the form of quantitative patch test here employed could be expected to be more accurate as an index of clinical sensitivity than is any other form of cutaneous test usually employed; in particular, it should be more accurate than cutaneous tests undertaken to determine clinical sensitivity in such diseases as hay fever and asthma. Some of the reasons for the expectation of greater accuracy of quantitative serial patch tests in relation to clinical sensitivity are the following:

1. The patch test is applied directly to the skin, to the organ actually affected by the clinical disease (in contrast to the conditions obtaining in hay fever, in which the skin is tested in order to ascertain the clinical sensitivity not of the skin itself but of some other organ).

2 In the patch test, the mode of exposure is mere external application without trauma, i e., the test exposure rather closely approximates the mode of clinical exposure to the excitant

3 The positive reaction to a patch test is an exact duplication (in miniature) of the clinical disease

4 In the quantitative serial dilutions, as employed in the present study, the end point was determined at which each subject no longer reacted. In other words, it was possible to determine for each person with a fair degree of accuracy, the actual level of sensitivity of the cutaneous tissues at the particular time and site

In spite of all these factors which are in favor of the accuracy of quantitative patch testing with serial dilutions as an index of clinical susceptibility, it is to be recalled that the conditions of natural exposure are nevertheless, different from those of any cutaneous test. It is, therefore, to be expected that there should be some divergence between the results of even the most accurate cutaneous tests possible and the results of actual clinical exposure of the skin to the natural excitant. Moreover, some of the discrepancies between patch test sensitivity and clinical susceptibility may be due to spontaneous chronologic variations in the skin's sensitivity to poison ivy, as well as to the local variations of degree of sensitivity in different areas of skin. The studies of Field and Sulzberger²⁵ have shown that both of these variables may be present in poison ivy sensitivity.

It is not to be expected, therefore, that the results of quantitative patch tests with serial dilutions will necessarily prove an absolute index of degree of susceptibility to subsequent clinical exposures. Nevertheless, whether one adopts the criterion of level of cutaneous sensitivity as determined by quantitative patch tests before and after specific injections or whether one considers only the influence of the injections on the incidence of subsequent clinical ivy dermatitis, it is evident that under the conditions of our experiments no noteworthy diminution of cutaneous sensitivity resulted from the injections of specific extract.

Due to the great divergence in results previously reported, the relation of our present findings to those of other observers is difficult to analyze. Our findings, that the specific injections produced no demonstrable reduction in the level of cutaneous sensitivity as determined by quantitative patch tests, seem to be beyond the influence of the fortuitous and fluctuating factors of clinical exposure and have already been confirmed by Simon and Lotspeich. Our results in regard to the effect of specific injections on the clinical incidence of ivy dermatitis are in accord with those of investigators who have been unable to show a

²⁵ Field, H., and Sulzberger, M. B. Experiments in Poison Ivy Sensitivity, *J. Allergy* 7:139 (Jan.) 1936

decided beneficial effect (for example, Zisserman and Birch²¹) and are in contrast to those of observers who have reported striking benefits (for example, Molitch and Poliakoff²⁶ and Blank and Coca¹⁸). The explanation for this discrepancy is not available, but it must be mentioned that the present findings, together with those of Zisserman and Birch, are in agreement as to the relative ineffectiveness of the specific measures employed.

Our results, moreover, and those of Zisserman and Birch were obtained independently in two large and adequately controlled series in which the subjects first received specific injections and were then allowed to have fairly massive exposures under natural conditions and without special protection. It may be that the degree of clinical exposure is an important determining factor and that if our patients had been less exposed or if they had been protected in the same manner as the subjects of Molitsch and Poliakoff or of Blank and Coca, the beneficial effects of specific prophylactic injections might have been apparent. At any rate, further studies in this direction are urgently required; and, in view of the fundamental nature of this problem, it would certainly seem indicated to carry out studies on large numbers of subjects receiving specific injections and of equal numbers of control subjects, having both groups subjected to various degrees of natural clinical exposures, both with and without protective measures.

The final judgment on the possible efficacy of specific injections in the prophylaxis of clinical ivy dermatitis must remain in abeyance until further studies have revealed the causes of the divergent findings on the part of different observers. Nevertheless, the demonstration by Simon and Lotspeich and by us that the specific injections fail to produce a regular reduction in the level of cutaneous sensitivity to poison ivy, as determined by quantitative patch tests, cannot simply be ignored. Our present findings at least indicate that any reduction of sensitivity which specific injections may produce are not of such degree or of such kind as to alter greatly the level of cutaneous sensitivity to either patch tests or to massive natural exposures in the majority of subjects. The foregoing statement, i.e., that the results of patch tests cannot be entirely ignored in any discussion of clinical susceptibility, is amply borne out by the results of the following two experiments. The results of these experiments (experiments 3 and 4) show that there is an undeniable relation between reactions to patch tests and both prior and subsequent clinical susceptibility to dermatitis on natural exposures.

Experiment 3.—It was attempted to study the question of the relation between positive reactions to patch tests with poison ivy extracts and previous clinical susceptibility to poison ivy dermatitis. For this purpose,

26. Molitch and Poliakoff (footnotes 17 and 19).

we divided our patients into two groups, the first group comprising 184 subjects with positive reactions to patch tests with one or more of the dilutions in the first series, and the second group comprising 198 subjects with negative reactions to the patch tests with all dilutions (experiment 1)

For the men of both these groups, a careful history was taken for previous clinical poison ivy dermatitis²⁷ Among the 184 subjects with positive reactions to patch tests, 92 (50 per cent) had a history of ivy dermatitis, in the group of 198 with negative reactions to patch tests, only 29 (14 per cent) had a history of previous ivy dermatitis

On the basis of these figures, there is an evident correlation between the incidence of positive reactions to patch tests with poison ivy extract and the incidence of a history of poison ivy dermatitis The reaction to patch tests is therefore in this respect a general index of previous clinical susceptibility to natural exposures

Experiment 4—The question of the relation between positive reactions to patch tests with poison ivy extracts and the subsequent clinical susceptibility to poison ivy dermatitis was studied

For this purpose, the 278 subjects who remained and could be observed during the entire duration of the experiment were divided into two groups (regardless of the injections received) The first group consisted of 119 men who had given positive reactions to one or more patch tests, the second group consisted of 159 persons who had given negative reactions to all patch tests The men in both groups were instructed in identical manner and subjected to approximately equal clinical exposures to the poison ivy plant, as outlined in experiment 1

In the group of 119 reactors to patch tests, there subsequently developed 36 cases of clinical dermatitis, an incidence of about 30 per cent In the group of 159 subjects with negative reactions to the patch tests, there subsequently developed 14 cases of clinical ivy dermatitis, an incidence of about 9 per cent²⁸

27 We know that the reliability of the statements made by these men regarding the history of previous rhus eruption may be suspected On the other hand, the majority of the persons in these particular camps were from rural districts, and they were probably accurately aware of the nature of an eruption when the cause was the poison ivy

28 In a separate experiment, for comparative purposes, additional patch tests were performed on 16 persons (selected arbitrarily in the course of the first series of patch tests), using an extract other than the one used in our experiment. This other extract was apparently stronger, because 2 persons showed positive reactions who did not react to the extract used in our experiment, and all the others gave qualitatively stronger reactions This points to the probability that with a stronger extract a greater correlation might have been attained than that reported (experiment 4) It also demonstrates that the use of different extracts by different observers is a cause for the divergent results obtained by them and indicates the need for a standard potent extract

There is an evident correlation between the incidence of positive reactions to patch tests with poison ivy extract and the incidence of clinical ivy dermatitis on subsequent exposures. The reaction to the patch test is therefore in this respect a general index of future clinical susceptibility to natural exposures.

SUMMARY AND CONCLUSIONS

The divergent results and contradictory opinions as to the efficacy of specific immunologic measures in the prophylaxis of poison ivy dermatitis are briefly discussed.

A method of cutaneous testing with quantitative serial dilutions of the excitant and the application of this quantitative method as an objective measure of the level of cutaneous sensitivity before and after the prophylactic injections are described.

The application of this quantitative method to measure the changes in the level of cutaneous sensitivity demonstrated that the specific injections did not succeed in producing a regular diminution of the skin's sensitivity, as demonstrable by patch tests. On the contrary, the quantitative patch tests demonstrated a slight increase in cutaneous sensitivity in the subjects specifically treated as contrasted with the controls.

A group of specifically treated subjects and a group treated with blank control injections were subjected to fairly massive natural exposures to *Rhus toxicodendron* during the six weeks following the injections. The natural exposures in both the treated and control groups were, on the whole, approximately identical. Under the conditions of this experiment, there was little difference in the incidence (or severity) of clinical ivy dermatitis in the two groups. Ivy dermatitis developed in 27 per cent of the specifically treated subjects and in 36 per cent of those who received control injections.

Some of the possible explanations of the lack of strict correlation between the results of quantitative patch tests and the clinical susceptibility to natural exposures are mentioned.

Some of the possible explanations of the divergent results of specific prophylaxis at the hands of various observers are discussed. The possible influence of various degrees of exposures in altering results is considered.

It is demonstrated that in a given group the results of patch tests with poison ivy extract are a general index of the incidence of previous clinical susceptibility to dermatitis from natural exposures to the plant.

It is demonstrated that in a given group the results of patch tests with poison ivy extract are a general index of the incidence of future clinical susceptibility to dermatitis from natural exposures to the plant.

VERRUCA PLANTARIS

EDWARD A OLIVER, MD

CHICAGO

Plantar warts are generally classed as minor dermatologic conditions, yet they are encountered so often and can be so troublesome that I believe a statistical review of the 516 cases I have had in my private practice may prove of value

Owing to the wide popularity of sports in America, necessitating the use of swimming pools, locker rooms, shower baths and bathing beaches, there has recently been a tremendous increase in the number of plantar warts

In an excellent paper published in 1919, Wile and Kingery¹ settled the question of the infectiousness of warts. They produced lesions of verruca vulgaris, which were both clinically and histologically typical, by injecting intracutaneously a sterile filtrate of wart material.

MacKenna² recently reported a widespread epidemic of plantar warts among English school children, especially adolescent girls. He stated the belief that individual susceptibility varies greatly but that the virus can secure a foothold on the skin where no abrasion can be seen. This virus probably cannot live or multiply except on living cells but may remain alive, presumably for some minutes if not hours, on a surface, such as a bath mat, where an affected foot has pressed.

A plantar wart is a papillomatous tumor formed of a thickened stratum mucosum and stratum corneum, overlying hypertrophied papillae which contain enlarged and dilated blood vessels.³ These vessels are easily ruptured, and the blood from the tops of the papillae leaks into the basal cell layer and is carried upward in the growing epidermic cells. In practically every wart there is seen a group of black points, which are small masses of blood pigment. The finding of these small black puncta is one means of differentiating warts from two other common conditions of the foot, namely, callosities and corns.

Plantar warts in most cases cause a great deal of pain. This may vary from an ordinary amount after prolonged walking to pain severe

President's Address, Chicago Dermatological Society, Jan 13, 1940

1 Wile, U J, and Kingery, L B. Etiology of Common Warts, J A M A 73 970 (Sept 27) 1919

2 MacKenna, R M B. Brit M J 1 509, 1938

3 Whitfield, A W. Brit J Dermat 44 580, 1932

enough to confine the patient to bed. In warts the pain ceases as soon as pressure is removed, while with corns the pain may occur even when the patient is in bed.

The treatment of plantar warts is one of the most important and difficult problems of the dermatologist. Methods used for treatment include surgical excision,⁴ surgical diathermy, curettage, electrolysis, freezing with solid carbon dioxide, application of salicylic acid plaster, suggestion, application of various acids and injections of a bismuth compound, both directly into the wart and intramuscularly. Probably the method of choice is the use of roentgen rays⁵ and of radium.

In 1931 Osborne and Putnam⁶ reported their results in 322 cases of plantar warts. The vast majority of their patients were between the ages of 10 years and 40. Forty per cent were females and 60 per cent males. The conditions in 87.7 per cent of their cases were cured by roentgen rays alone; in 80 per cent with one treatment and in 7.7 per cent with two treatments. They reported that they no longer used radium because of the time required. They stated that careful attention should be paid to the peripheral vascular condition of the patient, because failure to cure occurs more commonly in patients with a damaged vascular system than in any other kind of person.

Taussig and Miller⁷ reported that over 80 per cent of plantar warts were amenable to radiation therapy. They stated the belief that in the use of radium the maximum dose should be administered at the first application and treatment should not be repeated more than once. It was their impression that the roentgen ray dose should consist of an intensive application followed by two subintensive exposures at two week intervals. Their results were as follows: Eighty-one and eight-tenths per cent of the patients treated by roentgen rays were cured, and 88.6 per cent of those treated by radium, but only 53 per cent of those treated by combined roentgen ray and radium therapy.

Hazen⁸ reported his results in 157 cases. Roentgen rays alone were used in 136 cases, radium with roentgen rays in 21 cases, and radium alone in 6 cases. Among the 120 cases in which the final results were known, there were 8 failures. When roentgen ray and radium treatment were combined, there were but 5 failures. Nearly two thirds of his patients had previously been treated by chiropractors.

In my series of cases there were 276 children and 240 adults, a total of 516. The final results are known in 238 cases among the children

4. Haldin-Davis, H.: *Brit. M. J.* **2**:18 (July 2) 1938.

5. Michael, J. C.: *Roentgen-Ray Treatment of Verucca Plantaris*, *Arch. Dermat. & Syph.* **13**:658 (May) 1926.

6. Osborne, E. D., and Putnam, E. D.: *Radiology* **16**:340, 1931.

7. Taussig, L. R., and Miller, H. E.: *Am. J. Roentgenol.* **20**:514, 1928.

8. Hazen, H. H.: *Am. J. Roentgenol.* **19**:440, 1927.

and in 156 among adults, a total of 394. For 38 children and 84 adults the results are unknown, because some made only a single visit to the office.

There were 168 females and 108 males in the group of children. Their ages varied from 4 years to 17. The majority ranged in age from 12 to 15.

One hundred and twenty-three children had one roentgen ray exposure

106 had 3 skin units (1,050 r)
9 had $2\frac{1}{2}$ skin units (875 r)
8 had 2 skin units (700 r)

Unfiltered roentgen therapy was used in all these cases. There were 2 failures in the 123 cases, or 98.3 per cent successful results.

Twenty-nine children had two roentgen ray exposures

18 had 3 skin units (1,050 r)
5 had $2\frac{1}{2}$ skin units (850 r)
3 had 2 skin units (700 r)
3 had $1\frac{1}{2}$ skin units (525 r)

There were 3 failures in this group, or 89.6 per cent successful results.

When more than one roentgen ray exposure was given, the second treatment was not given until eight weeks had elapsed.

Sixty-four children were treated with one radium exposure, varying in time from one and one-half to two hours, depending on the depth of the lesion. A 10 mg plaque of full strength radium, shielded with 0.2 mm of aluminum and rubber, was placed directly in contact with the wart, after the surrounding skin had been shielded with lead foil. Radium was used mainly where there were multiple lesions. The results in this group were extremely satisfactory, in fact 100 per cent successful. Four children had two radium exposures, eight weeks apart. There was 1 failure in this group, giving 75 per cent successful results.

Five children were treated with both radium and roentgen rays. In addition to one radium treatment, 3 had two roentgen ray treatments of $1\frac{1}{2}$ skin units (525 r). Two had two roentgen rays treatments of 2 skin units (700 r) at eight week intervals.

Because of superficial and multiple lesions, 4 were treated by first applying a piece of 40 per cent salicylic acid plaster to the wart for several weeks and then curetting out the remainder of the lesion or cauterizing it. The results in 3 cases were good.

In 9 cases salicylic acid plaster, cautery, curettage and freezing with solid carbon dioxide were used because of previous roentgen ray therapy at the hands of another operator. In this group the results were only fair.

Thirty-eight children were not followed up. Fifteen had one roentgen ray treatment, 1 had two roentgen ray treatments, 17 had one radium treatment, 1 had two radium treatments and 4 were treated with salicylic acid plaster and cautery.

In the group of 240 adults there were 159 females and 81 males. One hundred and fifty-six cases were followed up and the results are known; in 84 cases the results are not known.

Forty-nine had a single roentgen ray treatment:

44 had 3 skin units (1,050 r)
 4 had $2\frac{1}{2}$ skin units (875 r)
 1 had 1 skin unit (350 r)

There were 4 poor results in this series, or 91.8 per cent successful results.

Twenty-six had two treatments with roentgen rays:

15 had 3 skin units (1,050 r)
 5 had 3 skin units plus $2\frac{1}{2}$ skin units (1,050 r and 875 r)
 1 had $2\frac{1}{2}$ skin units (875 r)
 5 had 2 skin units (700 r)

In this group there were 7 poor results, or 73 per cent successful results.

Thirty-five had one radium treatment of one and one-half to two hours, which gave 5 poor results, or 80.5 per cent successful results.

Six had two radium treatments of one and one-half to two hours, which gave 1 poor result, or 83.3 per cent successful results.

Fourteen had radium plus roentgen ray treatment:

5 had one radium treatment and one roentgen ray exposure of 3 skin units (1,050 r)
 2 had one radium treatment and two roentgen ray treatments of $2\frac{1}{2}$ skin units (875 r)
 4 had one radium treatment and two roentgen ray treatments of 2 skin units (700 r)
 3 had one radium treatment and two roentgen ray treatments of $1\frac{1}{2}$ skin units (525 r)

There were 3 poor results in this group.

Of the remaining 26 patients, 5 were treated with applications of salicylic acid plaster and solid carbon dioxide. Four had three roentgen ray treatments of $1\frac{1}{2}$ skin units, too small a dose. Three were treated with salicylic acid plaster applications and cautery, 4 with cautery alone, and for 9 that had had previous roentgen ray therapy before consulting me, solid carbon dioxide, cautery and salicylic acid plaster were the methods used.

I was unable to follow up 84 of the adult cases, and consequently the end results are unknown. Thirty-three of these had one roentgen ray treatment, 7 had two roentgen ray treatments, 30 had one radium treatment, 6 had two radium treatments, 5 were treated with radium and roentgen rays combined and 3 were treated with cautery.

Considering the results obtained with roentgen rays and radium, it would seem that the use of one or the other is the method of choice in the treatment of plantar warts. While it is true that excellent results have been obtained with other methods, namely surgical excision, removal with cutting current and electrolysis, one must remember that warts are infections caused by a virus and that there is always the possibility of opening up new channels of infection. Recurrences are common even after complete excision, and the possibility of producing scars must also be considered.

The use of roentgen rays is a method always welcomed by children, because there is no pain, no attendant fear of needles and knives and no interference with play. In children I believe it is always the method of choice, especially now with the use of shock-proof apparatus.

Radium is of the same value in children. The only objection to its use is the time element, but when there are numerous warts and enough radium is obtainable, a number of warts can be treated at one sitting.

It is of the utmost importance in the treatment of warts on the feet to see that the lesions are carefully shielded to their exact borders with lead foil. It is of equal importance that no more than two roentgen ray or two radium treatments be given to any one wart. These treatments should not be given oftener than seven or eight weeks. Following this method, I have not encountered a case of radiodermatitis, atrophy or keratosis, provided the wart had been shielded carefully. I believe that many of my early failures were due to the use of too small a dose of roentgen rays at the beginning of treatment. For children or for adults I believe that at least 3 skin units (1,050 r), provided the wart is carefully shielded, should be the initial dose.

For patients that have previously been treated elsewhere with roentgen rays and radium, I have used a 40 per cent salicylic acid plaster, with considerable success. I apply this for a week or two, until the wart has become soft, and then curet out what I can and freeze the remainder with solid carbon dioxide. This method is tedious, in that it requires a long time to effect a cure. Its advantages are that it is not painful and does not prevent the patient from pursuing his usual occupation.

The injection of a bismuth compound, either intramuscularly or directly into the wart, has been disappointing in the few cases in which I have used it. Suggestion therapy has been practiced with considerable success by Sulzberger and Wolf,⁹ Bloch,¹⁰ Jadassohn,¹¹ and others.

9 Sulzberger, M. B., and Wolf, J. *M. Rec.* **140** 552 (Nov. 21) 1934.

10 Bloch, B., cited by Sulzberger and Wolf.⁹

11 Jadassohn, J., cited by Sulzberger and Wolf.⁹

I have never tried it, but it is possible that some of my successful results with children may have been due in part to suggestion.

The attendant pain and disability make plantar warts more than a minor dermatologic condition. Most of them will respond to roentgen ray therapy; a few will resist it. I believe it to be safe practice to have the resistant lesions removed surgically or by some other means if after two roentgen ray exposures, given at intervals of eight weeks, they have not disappeared. In unexperienced hands roentgen ray therapy is dangerous, and its careless use can cripple a patient for life. If given properly it is one of the best weapons for removing this troublesome condition.

GENTIAN VIOLET IN SABOURAUD'S MEDIUM FOR ISOLATION OF PATHOGENIC FUNGI

S S EPSTEIN, PH D

AND

FOSTER DEE SNELL, PH D

BROOKLYN

In the usual diagnosis of dermatophytosis ("athlete's foot") scrapings from lesions are examined microscopically for the presence of fungi and inoculated into suitable medium for isolation of suspected strains. The finding of fungi depends largely on proper selection of material. Frequently material loaded with mycelia and spores may not yield a growth of fungi on the planted medium owing to overgrowth of bacterial contamination. To overcome such difficulty, it was found that plain Sabouraud dextrose-peptone medium containing 0.0002 per cent (1:500,000) gentian violet inhibited the growth of the usual bacterial flora of the skin without hindering the growth of pathogenic molds.

Records of a New York mycologic clinic¹ indicated that in approximately 25 per cent of clinical cases of fungous lesions the diagnosis was confirmed by microscopic examination and that in only 50 to 60 per cent of the cases in which the diagnosis was microscopically proved were suspected fungi yielded on slants of plain Sabouraud's medium. The medium employed consisted of 4 per cent dextrose, 1 per cent peptone (Fairchild) and 2 per cent agar.

Muskatblit and Director² in 1933 found fungi microscopically or in culture in 119 of 300 (39.7 per cent) clinical cases of dermatophytosis. Fifty clinical cases gave negative results on laboratory examination.

In the same year Legge, Bonar and Templeton³ obtained 244 cultures from 625 patients afflicted with dermatophytosis. The high percentage (39 per cent) of isolations was attributed in part to the large

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1 Lewis, G. M., and Hopper, M. E., Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital. Personal communication to the authors, 1938.

2 Muskatblit, E., and Director, W. The Trichophyton Test. Report of Three Hundred and Fifty Cases, Arch. Dermat. & Syph. 27:739-744 (May) 1933.

3 Legge, R. T., Bonar, L., and Templeton, H. J. Epidermomycosis at the University of California, Arch. Dermat. & Syph. 27:12-24 (Jan) 1933.

number of inoculations per lesion and in part to the medium employed. These investigators used a peptone-free medium of the following composition: potassium acid phosphate (KH_2PO_4) 1.2 Gm., magnesium sulfate 0.5 Gm., dextrose 6 Gm., desiccated malt extract 6 Gm., agar 20 Gm. and distilled water 1,000cc. Fungi were found to grow readily on this medium and bacteria less readily than on Sabouraud's dextrose-peptone medium.

Farley⁴ in 1920 found that with stock cultures 0.0004 and 0.0002 per cent gentian violet in solid maltose mediums restrained the growth of gram-positive bacteria but not of molds. He used such mediums with good results in isolating 20 strains of pathogenic molds.

During the progress of the present study Ch'in⁵ in 1938 reported that Sabouraud medium containing 0.015 per cent potassium tellurite or 0.05 per cent cupric sulfate was definitely superior to plain Sabouraud medium in the primary isolation of pathogenic fungi, as based on fifty tests with experimental material taken directly from lesions known to be due to fungous infection. Such mediums suppress the growth of bacteria but not of fungi. With potassium tellurite the initial growths of fungi were black. Color characteristics and colonial appearances were resumed on transfer to plain Sabouraud medium.

The bacteriostatic effect of gentian violet on gram-positive bacteria has been long known. As early as 1912 Churchman⁶ found that a majority of gram-positive bacteria were inhibited in their growth by gentian violet. The work of Farley⁴ in 1920 indicated the useful application of this dye in mediums for molds. Therefore, two basic mediums, adjusted to various hydrogen ion concentrations and containing different minute quantities of gentian violet, were tested for the growth of Trichophyton strains and composite bacterial flora from pathogenic skin. Ordinary Sabouraud's medium (4 per cent dextrose, 1 per cent Fairchild's peptone and 2 per cent agar)¹ and the peptone-free dextrose medium of Legge, Bonar and Templeton,³ with p_H values of 5.2, 5.4, 5.6, 5.8 and 6 and containing 0.001, 0.0004, 0.0002 and 0.0001 per cent gentian violet, were heavily inoculated with stock Trichophyton (Trichophyton interdigitale and Trichophyton rosaceum) cultures, with and without added heavy bacterial contamination and also with primary impure growths of Trichophyton molds arising from human infectious

4. Farley, D. L.: The Use of Gentian-Violet as a Restrainer in the Isolation of Pathogenic Molds, Arch. Dermat. & Syph. 2:459-465 (Oct.) 1920.

5. Ch'in, T. L.: Potassium Tellurite and Copper Sulfate in Sabouraud's Medium for Isolation of Pathogenic Fungi, Proc. Soc. Exper. Biol. & Med. 38: 700-702, 1938.

6. Churchman, J. W.: The Selective Bactericidal Action of Gentian Violet, J. Exper. Med. 16:221-247, 1912.

materials The inoculated tubes (15 cc of medium slanted in 25 by 150 mm culture tubes) were kept at room temperature Observations and records were frequently made

The results clearly indicated that gentian violet in all the mediums previously mentioned markedly inhibited the growth of the usual bacterial flora of the skin without hindering the growth of Trichophyton molds Best results were observed in plain Sabouraud medium at a p_H

TABLE 1—*Merits of Sabouraud Medium, Plain and with Gentian Violet, in Isolating Eighty-Eight Strains of Pathogenic Fungi*

Cultivation	Number of Strains Isolated	Plain Sabouraud Medium		Sabouraud Medium with Gentian Violet	
		Number	Per Cent	Number	Per Cent
Initial	44	33	75 0	42	95 5
Later	44	36	81 8	44	100 0
Total	88	69	80 7	86	97 7

TABLE 2—*Comparison of Plain Sabouraud Medium with Sabouraud Medium with Gentian Violet in Preliminary Cultivation of Materials from Lesions of Clinical Dermatophytosis*

	Specimens from Which Fungi Were Isolated				Specimens Which Were Microscopically Positive and from Which Fungi Were Not Isolated				Specimens Which Were Microscopically Negative and from Which Fungi Were Not Isolated			
	Plain		With Gentian Violet		Plain		With Gentian Violet		Plain		With Gentian Violet	
	Num ber	Per Cent	Num ber	Per Cent	Num ber	Per Cent	Num ber	Per Cent	Num ber	Per Cent	Num ber	Per Cent
Fungous Growth												
Good to heavy	36	52 2	57	66 3								
Fair	33	47 8	29	33 7								
Bacterial Growth												
Good to heavy	45	65 2	4	4 7	45	81 8	0	0	74	66 5	7	62 2
Slight to fair	22	31 9	53	67 4	10	18 2	32	84 2	39	34 5	91	80 5
None	2	2 9	24	27 9	0	0	6	15 8	0	0	15	13 3

of 5 8 prior to sterilization and containing 0 0002 per cent (1 500,000) gentian violet This concentration of dye also definitely retarded the growth of stock cultures of a number of sporulating and nonsporulating yeasts It was interesting to note that growth of molds as well as of bacteria was slower and less intense on peptone-free mediums than on peptone mediums

The merits of Sabouraud dextrose-peptone-agar mediums containing 0 0002 per cent gentian violet as compared with those of plain Sabouraud medium for isolating pathogenic fungi were based on simultaneous inoculations of materials from clinically diagnosed dermatophytosis

lesions of 131 patients. These patients were inmates of an orphan asylum wherein a survey of the prevalence of dermatophytosis was made. The infection was observed in 40.1 per cent of 327 persons examined by a medical official of the institution.

In the mycologic diagnosis in the 131 cases of clinical dermatophytosis, 62 (47.3 per cent) of the lesions gave positive results microscopically or in culture. Forty-four (33.6 per cent) of the lesions gave positive results in culture, of which 43 (32.8 per cent) also gave positive results microscopically. Eighteen (13.7 per cent) gave positive results microscopically and negative results in culture.

Of the 44 fungi isolated, 33 (75 per cent) were obtained on plain Sabouraud medium, as compared with 42 (95.5 per cent) successful isolations with Sabouraud medium containing gentian violet. In 2 instances materials yielded growth on plain Sabouraud medium and not on the dye medium, while in 11 other instances cultures were obtained on the dye medium and not on plain Sabouraud agar. The fungi isolated in this study included *Epidermophyton interdigitale* (T. interdigitale) (39), *T. rosaceum* (2), *Epidermophyton rubrum* (2) and *Monilia albicans* (1).

During a course of treatment over a period of three to fourteen months numerous mycologically proved lesions were reexamined. Table 1 shows that a total of 88 strains were obtained by the simultaneous use of both mediums. The results indicate that over 19 per cent of the positive findings would not have become available had sole reliance been placed on plain Sabouraud dextrose-peptone agar for isolation of fungi from clinical lesions of dermatophytosis.

A total of 237 specimens were cultivated, of which 88 (37 per cent) yielded fungi on either or both of the mediums. Records of observations relative to growth of molds and bacteria are presented in table 2.

From table 2 it will be noted that Sabouraud medium containing 0.0002 per cent (1:500,000) gentian violet for primary isolation of fungi is definitely superior to ordinary Sabouraud medium. It not only yielded more positive cultures, but it also simplified subsequent purification, because of decidedly less bacterial interference.

305 Washington Street.

ACUTE INTERSTITIAL MYOCARDITIS FOLLOWING ADMINISTRATION OF ARSPHENAMINES

CLARK E BROWN, M D

AND

DELBERT H McNAMARA, M D

SANTA BARBARA, CALIF

The fatal acute cardiac failure which sometimes intervenes during the course of exfoliative dermatitis due to arspenamine is seldom anticipated clinically, and the microscopic appearance of the myocardium post mortem is even less expected

The cases of such myocardial changes following the onset of arspenamine dermatitis comprise part of the general group of instances of a condition designated as acute interstitial, isolated or Fiedler's myocarditis. The more than 40 recorded cases making up this general group have in common the apparently spontaneous occurrence of progressive myocardial failure and diffuse interstitial inflammation involving a thickened left ventricular myocardium according to post-mortem observations

Fiedler in 1899 called attention to this peculiar nonspecific interstitial myocarditis accounts of which first reached the American literature in 1929 with a review by Scott and Saphir¹. They collected 30 cases and added 2 of their own but did not include Fiedler's cases because of their relative inaccessibility. They noted, however, that Steffen reported the first case in 1888.

During the past ten years occasional reports have appeared on acute interstitial myocarditis. Nelson² in 1934 reported on a patient in whom a myocarditis of the interstitial type developed while exfoliative dermatitis due to neoarsphenamine was present. Nelson was the first to single out arsenical dermatitis as an etiologic factor, although cutaneous infection in general had been implicated as a cause of the myocardial injury by Bailey and Anderson³ three years before.

From the Departments of Pathology and Internal Medicine of the Santa Barbara Cottage Hospital

1 Scott, R W, and Saphir, O. Acute Isolated Myocarditis, *Am Heart J* 5 129 1929

2 Nelson R L. Acute Diffuse Myocarditis Following Exfoliative Dermatitis, *Am Heart J* 9 813, 1934

3 Bailey F R, and Anderson, D H. Acute Interstitial Myocarditis, *Am Heart J* 6 338 1931

In 1936 Sikl⁴ assembled 5 cases of interstitial myocarditis complicating dermatitis due to arsphenamine. He described in addition a case of his own, particularly as regards the type of cellular exudate, which was predominantly eosinophilic. In addition, necrotic foci containing epithelioid cells and giant cells were noted in the myocardium, within which neither tubercle bacilli nor spirochetes could be demonstrated. Sikl discussed in detail a similar case of Fingerland,⁵ a report of which subsequently appeared in the Czechoslovakian literature. In Fingerland's case the myocardium contained numerous so-called tuberculoid foci, as well as a diffuse interstitial cellular exudate, of which eosinophils constituted a considerable proportion. Sikl also discovered in the literature a case of polymyositis and myocarditis following administration of neoarsphenamine, reported by von Zalka,⁶ and 2 cases of fatal myocarditis due to arsphenamine, reported by Stoeckenius.⁷ Stoeckenius had presented these 2 in a group of 4 cases of what he interpreted as exacerbations of the syphilitic process under arsphenamine therapy. He indicated that in only 1 of these were changes noted that could be construed as suggesting chronic arsenic poisoning. The myocardial lesions were essentially similar to those aforementioned, as well as to those in Nelson's case. Sikl pointed out that the lesions exhibiting eosinophilic exudate and tuberculoid foci were similar to allergic lesions in general and advanced the hypothesis that myocarditis developed as an allergic reaction to arsphenamine.

In 1936 Taussig and Oppenheimer⁸ reported a case of myocarditis following antisyphilitic therapy, which resembled some of those collected by Sikl sufficiently to be included in this group. A child suffering from sickle cell anemia and transfusion syphilis was given nine injections of sulfarsphenamine intramuscularly. During the course of treatment a rash developed and she died of acute cardiac decompensation. Tubercle-like coalescent foci of necrosis with giant cells were noted in the myocardium, liver, lungs and lymph nodes. The authors concluded that the lesions were probably due to syphilis, although exhaustive attempts to demonstrate spirochetes gave negative results.

4. Sikl, H.: Eosinophile Myocarditis als idiosynkrasische-allergische Erkrankung, Frankfurt. Ztschr. f. Path. **49**:283, 1936.

5. Fingerland, A.: Allergic Nature of Arteritis, Periarteritis, Myocarditis, and Dermatitis Following Arsphenamine Therapy, Časop. lék. česk. **76**:359 and 404, 1937. A translation is not accessible.

6. von Zalka, E.: Ueber einen seltsamen Fall von Polymyositis, Virchows Arch. f. path. Anat. **281**:114, 1931.

7. Stoeckenius, W.: Beobachtungen an Todesfällen bei frischer Syphilis, Beitr. z. path. Anat. u. z. allg. Path. **68**:185, 1921.

8. Taussig, H. B., and Oppenheimer, E. H.: Severe Myocarditis of Unknown Etiology, Bull. Johns Hopkins Hosp. **59**:155, 1936.

Our case is offered as an example of acute interstitial myocarditis of the eosinophilic type complicating exfoliative dermatitis from neoarsphenamine used in the treatment of syphilis

REPORT OF A CASE

A white man aged 34 was admitted to the Santa Barbara Cottage Hospital on June 29, 1938, with acute exfoliative dermatitis of two days' duration. On March 25 a tonsillectomy had been performed, at which time the patient presented reports of negative results of Kolmer and Hinton serologic tests performed elsewhere one month previously. On May 2 the patient visited his physician because of a sore throat and a generalized rash typical of secondary syphilis. The Kolmer and Kahn reactions at this time were 4 plus. He received biweekly injections of 0.6 Gm of neoarsphenamine for six doses, with complete disappearance of the cutaneous lesions and throat symptoms at the end of the second week. The patient then received four weekly doses of an aqueous suspension of metallic bismuth (bismoid), 1 cc intramuscularly. After the fourth injection a mild itching erythematous rash developed on all cutaneous surfaces except those of the face, hands and feet. Administration of the bismuth compound was discontinued, and the rash improved. One week later, while he was apparently in good health, the patient received 0.6 Gm of neoarsphenamine. Two days later a generalized dermatitis developed, which became so severe within forty-eight hours that he was admitted to the hospital. The urine was essentially normal, and a blood count was not performed. Physical examination showed him to be acutely ill, with his skin covered with a rash characterized by coalescing wheals, with intense subcutaneous and submucosal edema, most severe in the mouth and on the face, neck and upper extremities. Therapeutic measures included intravenous injections of sodium thio-sulfate, and during the next three days progress seemed satisfactory except for nausea and vomiting occasionally. The temperature varied from 101 to 103 F and the pulse rate from 90 to 100, and the respiratory rate was 20 per minute. On the morning of the fourth day in the hospital and the sixth day of his rash he suddenly became cyanotic, dyspneic and apprehensive. The pulse became weak and rapid, and the respiratory rate rose to 40 per minute. The blood pressure was 70 systolic and 50 diastolic, and the temperature rose to 105.2 F by rectum. In spite of infusions of dextrose solution and hypodermic injections of ephedrine, the blood pressure remained low. Repeated sponge baths and colonic irrigations failed to lower the temperature. The signs of cardiac decompensation increased, and the patient died fifteen hours after onset of symptoms of myocardial failure.

Postmortem Examination—An autopsy was performed ten and one-half hours after death. The body was 5 feet and 8 inches (173 cm) tall and weighed about 160 pounds (73 Kg). The striking feature of the external appearance was a morbilliform macular rash on the face, trunk and abdomen and to a lesser extent on the extremities. Purulent crusts covered the lesions on the face and scalp. The skin of the cheeks and neck showed a dusky erythematous change and moderate subcutaneous edema. Clear, thin fluid (1,500 cc) was present in the peritoneal cavity, and the retroperitoneal fat was edematous. Each pleural cavity contained 200 cc of clear fluid. The pericardium was normal.

Heart The heart weighed 470 Gm. The myocardium of the left ventricle and septum on section showed irregular dull yellow firm patches with raised edges. The intervening myocardial fibers had a fine yellowish gray appearance. The entire myocardium was stiff and tense and had a "parboiled" consistency. The endo-

cardium was smooth, and the valves were delicate. The coronary arteries were soft and patent throughout. The aorta was soft and elastic and had a smooth intima.

Lungs: The right lung weighed 530 Gm. and the left 470 Gm. All lobes were crepitant, but the cut surfaces oozed dark blood.

Gastrointestinal Tract: The gastrointestinal tract was normal.

Liver: The liver weighed 1,890 Gm. The capsule was smooth and tense, and the cut surface showed swollen, yellowish lobular markings, accentuated by the adjacent dark sinusoids. The gallbladder and bile ducts were normal.

Spleen: The weight of the spleen was 300 Gm. The capsule was tense, and the pulp was soft, red and bloody. The follicles were swollen.

Kidneys: The right kidney weighed 195 Gm. and the left 175 Gm. They were similar and appeared normal except for swollen cortical markings. The ureters, genitalia, bladder, pancreas, adrenals, lymph nodes and skeleton were not remarkable.

Brain: The brain weighed 1,450 Gm. The meninges were smooth and delicate. The convolutional and sectioned surfaces of the hemispheres and cerebellum displayed only capillary engorgement. The basal vessels were soft and patent. The pituitary gland, weighing 0.446 Gm., and the pineal body were normal.

Microscopic Examination.—Heart: All sections of the left ventricular myocardium showed a generalized infiltration of eosinophils and round cells between the muscle fibers. In places the exudate was so heavy that it crowded out the adjacent muscle fibers. Severe edema with scattered red cells and fibrin accompanied the leukocytic exudation. The proportion of cells present in the exudate was approximately as follows: 55 per cent eosinophils, 28 per cent histiocytes or fibroblasts, 13 per cent lymphocytes, including plasma cells, and 4 per cent neutrophils (fig. 1). Scattered small foci were noted, in which the histiocytes and fibroblasts were closely packed together about necrotic centers (fig. 2). These scattered foci of necrosis and basophilic macrophages suggested an early stage of what Sisk called "tuberculoid foci." The eosinophils were distributed generally. The blood vessels appeared normal, and the interstitial cellular exudate seemed to have no tendency to perivascular arrangement. The muscle fibers usually displayed only severe pressure atrophy, but in parts a number of them were opaque, amorphous and eosinophilic, indicating necrosis. The right ventricle exhibited similar but less extensive cellular infiltrates, but both auricles were normal. Spirochetal and bacterial stains gave negative results.⁹

The remainder of the organs showed passive congestion. The sections of voluntary muscle and of the brain were normal.

Summary: The microscopic observations indicated acute and subacute interstitial myocarditis, passive congestion of the lungs and liver with central necrosis of the liver, acute splenic tumor, cloudy swelling of the kidneys and exfoliative dermatitis.

COMMENT

Since arsenical exfoliative dermatitis is considered to be an allergic manifestation on both clinical¹⁰ and on experimental grounds,¹¹ it

9. Dr. Carl Weller confirmed the absence of spirochetes in the myocardium and expressed the opinion that the myocardial reaction was essentially nonsyphilitic.

10. Tuft, L.: *Clinical Allergy*, Philadelphia, W. B. Saunders Company, 1938, p. 154.

11. Frei, W.: *Modern Clinical Syphilology*, *ibid.*, 1928, p. 334.

Substanzen, *Klin. Wchnschr.* 7:1026, 1928.



Fig 1—Acute interstitial myocarditis due to neoarsphenamine. Note the generalized interstitial edema, hemorrhage and exudate. The muscle fibers appear atrophied and disrupted as though from pressure. The vessel shows little change ($\times 108$)

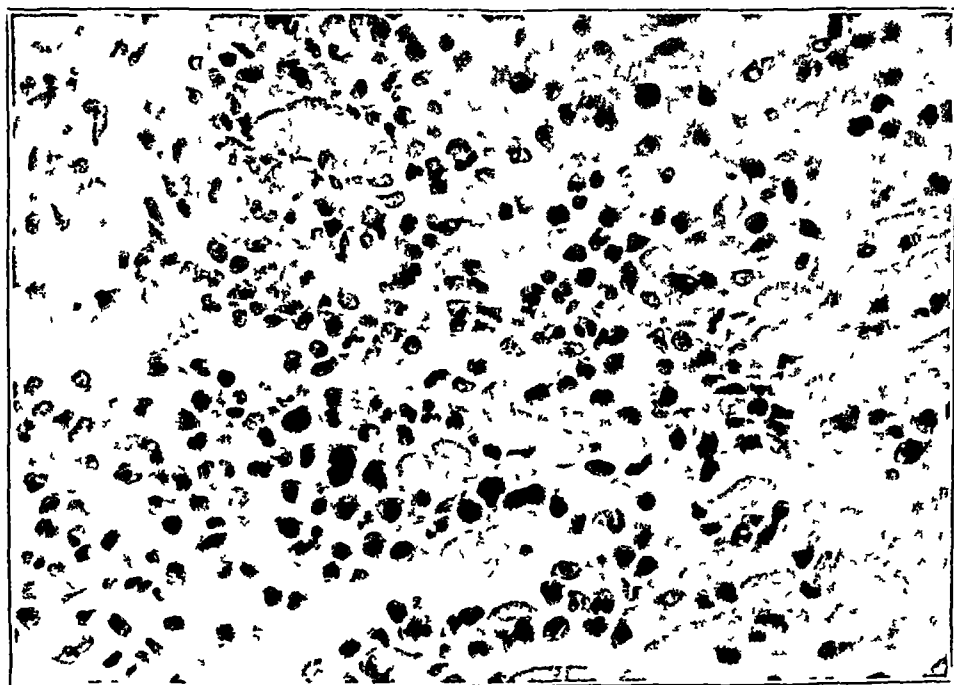


Fig 2—Acute interstitial myocarditis due to neoarsphenamine. This section is taken through a focus of muscle necrosis. Note the numerous basophilic histiocytes and the predominance of eosinophils in the exudate. Foci of muscle necrosis are minute and scattered ($\times 450$)

is reasonable to assume that complicating visceral lesions may have a similar pathogenesis. Allergic visceral lesions are thought to result from both chemical and bacterial idiosyncrasy. Good circumstantial evidence suggests that hepatic lesions may develop from drug allergy (cinchophen).¹² In rheumatic fever the myocardium is thought to display its capacity for bacterial allergic response with the development of the Aschoff body.

The experimental observations of some investigators constitute pertinent data on the implication of the myocardium in certain allergic reactions. Klinge¹³ has produced in rabbits, by repeated intra-articular injections of small amounts of horse serum, valvular and myocardial foci of necrosis with giant cell infiltrations. The spontaneous development of lesions somewhat similar to these in rabbits, however, has been reported by Miller.¹⁴ Modified Arthus experiments by Seegal, Seegal and Jost¹⁵ have shown that the myocardium may be involved secondarily in frank pericardial allergic inflammations. The authors produced such an inflammation in rabbits by injection of egg albumin intrapericardially after five previous subcutaneous injections of the same protein.

Although all types of allergic tissue response are neither morphologically specific nor constant, a few points of similarity between some of them and the myocardial exudates due to arsphenamine are noteworthy. Eosinophils are prominent in most of these myocardial exudates. Kline, Cohen and Rudolph¹⁶ have shown this type of cell to be a constant and predominant component of the early local exudate following the intracutaneous injection of allergens in man. It should not be inferred, however, that all eosinophilic exudates in the myocardium involve an allergic mechanism. The tissue in figure 3 is from a patient with diphtheritic myocarditis. Eosinophils formed a considerable proportion of the exudate, a fact noted previously in the literature.¹⁷ It should be emphasized, however, that in diphtheria the fragmentation and hyaline necrosis of the cardiac musculature are intense and conspicuous and the interstitial exudate is limited more or less to the foci of necrosis. In arsenical myocarditis, on the other hand (figs.

12. Quick, A. J.: The Probable Allergic Nature of Cinchophen Poisoning, *Am. J. M. Sc.* **187**:115, 1934.

13. Klinge, F.: Ueber Rheumatismus, *Klin. Wehnschr.* **91**:586, 1930.

14. Miller, C. P., Jr.: Spontaneous Interstitial Myocarditis in Rabbits, *J. Exper. Med.* **40**:543, 1924.

15. Seegal, B.; Seegal, B. C., and Jost, E. L.: Arthus Phenomenon: Local Anaphylactic Inflammation in Rabbit Pericardium, Heart and Aorta, *J. Exper. Med.* **55**:155, 1932.

16. Kline, B. S.; Cohen, M. B., and Rudolph, J. A.: Histologic Changes in Allergic and Non-Allergic Wheals, *J. Allergy* **3**:531, 1932.

17. Boyd, W.: Pathology of Internal Diseases, Philadelphia, Lea & Febiger, 1936, p. 61.

1 and 2), the exudative changes are widespread and are apparently not secondary to the scanty and widely scattered necrotic muscle fibers

Brody and Smith,¹⁸ in a relatively recent review of visceral lesions caused by scarlet fever, observed myocardial involvement in 90 per cent of the cases. These lesions were characterized by focal necrosis and interstitial collections of round cells, resembling in part the exudate in arsphenamine myocarditis. Although the authors judged the myocardial reaction to result from the toxic action of remote streptococci, Rossle¹⁹ has suggested that the myocardial lesions due to scarlet fever are examples of allergic tissue response.

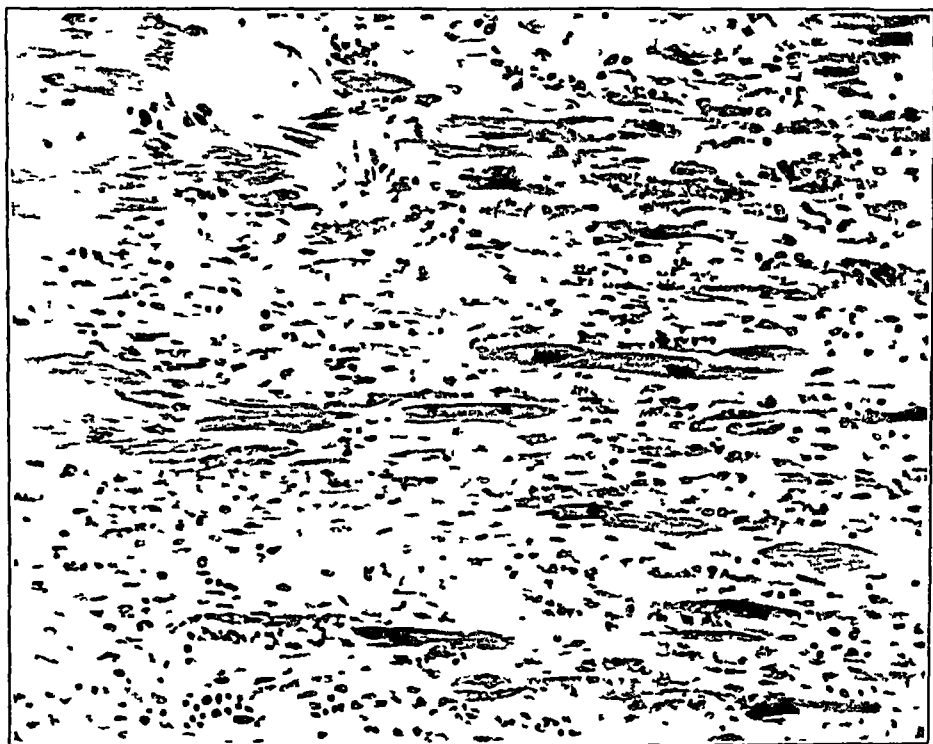


Fig 3—Diphtheritic myocarditis. In contrast to figure 2, note the extensive primary muscle necrosis. Edema is lacking, and exudate is minimal in proportion to the muscle damage. Many of the polymorphonuclear leukocytes are eosinophils ($\times 166$).

The granulomatous foci observed in the myocardium of many of the cases of myocarditis due to arsphenamine have a certain similarity to the early lesions of experimental tuberculosis. Dienes and Mallory²⁰

18 Brody, H., and Smith, L. W. The Visceral Pathology in Scarlet Fever and Related Streptococcus Infections, *Am J Path* **12**:373, 1936.

19 Rossle, R. Allergie und Pathergie, *Klin Wchnschr* **12** 574, 1933.

20 Dienes, L., and Mallory, T. B. The Influence of Allergy upon the Development of Early Tuberculous Lesions, *Am J Path* **13** 897, 1937.

have demonstrated in guinea pigs that the early monocytic granulomatous response to tubercle bacilli arises on an allergic basis.

Increased capillary permeability and hemorrhagic phenomena are observed frequently in the more acute and severe forms of tissue hypersusceptibility.²¹ While the diffuse myocardial hemorrhages seen in our case can be considered an allergic phenomenon, the well recognized direct toxic effect of arsphenamine on the capillaries might also account for the diffuse extravasations. In reviewing 44 autopsies among 63 fatalities due to arsphenamine, Cook²² indicated that hemorrhages into various organs, notably the brain, liver and kidneys, were conspicuous findings. In 6 autopsies severe congestion and hemorrhages into the myocardium were noted. Such changes, however, were apparently unaccompanied by the other types of exudate so conspicuous in our case.

The exclusion of bacteria or their toxins as causal factors of the myocarditis rests largely on indirect evidence. Cultural studies of the blood or myocardium unfortunately were not made in our case. On the other hand, the most highly inflammatory focus in our patient was the myocardium, and bacteria were not demonstrable at this site by specific tissue stains. This implies but, of course, does not prove that a bacterial endotoxin is not the causal factor involved. Regarding exotoxins, such an outspoken exudative myocardial reaction apparently has not been shown experimentally to have resulted from Dick scarlet fever toxin or clinically from diphtheria toxin in the absence of widespread muscle damage. The fact that our patient displayed a fever does not implicate bacteria, since this sign may even precede the appearance of the dermatitis.

In the light of our present knowledge, therefore, the acceptance of the allergy hypothesis to explain the myocardial lesions of arsphenamine dermatitis rests on the exclusion of other causes on morphologic grounds and on the compatibility of the lesions with those encountered in other types of known allergy. The preceding paragraphs have attempted to satisfy these provisions and to establish the hypothesis as an attractive possibility.

The source of the allergens is obscure. It would certainly be of academic interest to establish drug allergy (arsphenamine) as a direct cause of the myocardial reaction. If one accepts the dermal reaction to arsenic as a manifestation of allergy, there is no good reason to exclude a similar myocardial reaction from the realm of possibility.

21. Manwaring, W. H.; Hosepian, V. M., and Thomson, W. L.: Quantitative Study of Anaphylactic Capillary Permeability, *J. A. M. A.* **82**:542 (Feb. 16) 1924.
 22. Cook, S. S.: Postmortem Findings in Fatalities Due to the Use of the Arsphenamine Group, *Pub. Health Rep.* **51**:927, 1936.

Perhaps, as Kline and Young²³ have suggested, in other forms of visceral allergy lesions develop in the viscera because of the hyper-saturation of the derma with the allergen. On the other hand, in the general group of interstitial myocarditis, nonspecific dermatitis has been a conspicuous preliminary phenomenon.

Bailey and Anderson have emphasized the association of infection, especially pyogenic infections of the skin, and interstitial myocarditis in 11 of the 32 cases reviewed by them. In all cases of acute myocarditis due to arsphenamine recorded to date a generalized dermatitis has preceded the symptoms of cardiac insufficiency for between six and twenty days. In the case of Taussig and Oppenheimer there was a relatively mild cutaneous reaction, while in all the others the reaction was apparently severe. The constant anticipation of the myocardial changes by the dermatitis and their development in patients not receiving arsphenamine favor but do not establish the hypothesis that a factor associated with the dermatitis causes the subsequent myocarditis. In this concept the role of the drug is merely that of instigating the severe dermatitis, with the subsequent development of bacterial allergens. The possibility of an allergen arising from a combination of dermal infection and the arsenical must also be entertained.

Of interest here is the report of Maxwell and Barrett²⁴ concerning a patient in whom acute interstitial myocarditis developed more than two months after the onset of severe generalized dermatitis following the application of sulfur ointment for scabies. Septicemia unfortunately had intervened in the meantime. Here also the role of the drug is not clear.

Any discussion of acute myocardial inflammation found in a syphilitic person should include reference to the cases of malignant myocardial syphilis reported by Warthin²⁵. In these much of the exudative involvement was perivascular, and miliary gummas could be identified frequently. In addition to these, Boyd²⁶ has noted collections of neutrophils containing spirochetes in the left ventricular myocardium of a patient considered by him to have acute myocardial syphilis. In our case the ventricular exudate was diffuse and acute and lacked any perivascular arrangement. Syphilitic myocarditis would seem unlikely after apparent disappearance of general symptoms following initial neoarsphenamine therapy.

23 Kline, B. S., and Young, A. M. Normergic and Allergic Inflammation, *J. Allergy* **6** 247, 1935.

24 Maxwell, E. S., and Barrett, C. C. Acute Interstitial Myocarditis, *Arch. Dermat. & Syph.* **29** 382 (March) 1934.

25 Warthin, A. S. Primary Tissue Lesions in the Heart Produced by *Spirocheta Pallida*. *Am. J. M. Sc.* **147** 667 1914, Extensive Diffuse Myocarditis Associated with Malignant Syphilis, *Am. Heart J.* **14** 35, 1930.

26 Boyd, W. Acute Myocardial Syphilis, *Arch. Path.* **2** 340 (Sept.) 1926.

Bismuth has been excluded from the discussion purposely because of the lack of detailed data on its effects. Most of the reports trace the onset of the dermatitis directly to the arsenical, although a bismuth compound was included in the treatment. In our patient an initial mild eruption interrupted the course of administration of bismuth and was transformed with unusual suddenness into severe exfoliative dermatitis after the resumption of treatment with neoarsphenamine.

SUMMARY

A case of acute interstitial myocarditis complicating exfoliative dermatitis due to neoarsphenamine is reported. A similar case is reviewed in some detail, bringing the total cases reported to 8.

The probably allergic etiology of the myocarditis is discussed, although the exact nature of the allergen is not apparent.

EXUDATIVE CHRONIC DISCOID AND LICHENOID DERMATITIS (SULZBERGER AND GARBE)

TREATMENT OF FIVE PATIENTS

FRANCES PASCHER, M D

BROOKLYN

In 1937 Sulzberger and Garbe¹ described a group of cases of what they designated "distinctive exudative discoid and lichenoid chronic dermatosis." The authors referred to similar cases that had been described before with a variety of different diagnoses and also credited Rosen² with being the first to express the opinion that these cases may be examples of a distinctive dermatosis. Since Sulzberger and Garbe's publication, a number of cases with the diagnosis of exudative discoid and lichenoid chronic dermatosis have been presented before dermatologic societies,³ and a similar group of cases was studied by Cannon⁴. The latter author, however, referred to the condition in his cases as allergic dermatitis simulating lymphoblastoma. The characteristic features of the disease as it appeared in Sulzberger and Garbe's cases may be described as follows:

1 Chronic discoid and lichenoid dermatitis appears during the fourth or fifth decade of life and thus far has been observed only in Jewish males. There were 2 women and 1 gentile in the group as reported by Cannon.

2 The dermatitis is chronic and remittent and is associated with intense and intractable itching.

3 The eruption may be localized at first and later become generalized, or it may be generalized from the start. Not infrequently the

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

1 Sulzberger, M. B., and Garbe, W. Nine Cases of Distinctive Exudative Discoid and Lichenoid Chronic Dermatosis, *Arch. Dermat. & Syph.* **36**: 247 (Aug.) 1937.

2 Rosen, I., in discussion on Kaufman, S. M. Generalized Erythroderma, *Arch. Dermat. & Syph.* **32**: 962 (Dec.) 1935.

3 (a) Wright, C. S. A Case for Diagnosis (Exudative Discoid and Lichenoid Dermatosis), *Arch. Dermat. & Syph.* **37**: 525 (March) 1938. (b) Wise, F. Exudative Discoid and Lichenoid Chronic Dermatosis, *ibid.* **40**: 287 (Aug.) 1939. (c) Sulzberger, M. B. Exudative Discoid and Lichenoid Chronic Dermatosis, *ibid.* **40**: 288 (Aug.) 1939.

4 Cannon, A. B. Allergic Dermatitis Simulating Lymphoblastoma, *Arch. Dermat. & Syph.* **39**: 846 (May) 1939.

soles are the first areas to be affected, and the condition may closely resemble dermatophytosis. The entire integument becomes involved early in the course of the disease.

4. Several distinct types of lesions may be present at the same time or at any given time, or one type of lesion may predominate. Depending on the predominating lesions, Sulzberger and Garbe described (*a*) an exudative and discoid phase, in which the majority of lesions are made up of sharply demarcated discoid or irregular patches of exudation and crusting, which persist for varying lengths of time and when they undergo involution become dry, scaly, lichenified and pigmented; (*b*) a lichenoid phase, in which the majority of the lesions are made up of follicular lichenoid papules grouped in variously sized patches; (*c*) a phase resembling the premycotic stage of mycosis fungoides, in which the eruption is composed chiefly of infiltrated nodules and plaques, and (*d*) an urticarial phase (urticarial lesions may appear in showers throughout the course of the disease but are particularly prone to appear before a remission).

5. Clinical and laboratory investigation, including histologic examination of the skin, in these cases failed to shed light on the cause or pathogenesis of this dermatosis. The histologic observations did not seem to fit in with any known dermatologic entity.

6. Finally, the condition was found to be extremely refractory to treatment, with the exception of a tendency to temporary remission on change of environment, including hospitalization.

A report of 5 additional cases of this dermatosis is submitted to confirm the observations of Rosen, Sulzberger and Garbe and to present a method of treatment that proved to be successful in these cases.

The shortest duration of the illness in these 5 patients before the treatment to be described was begun was eighteen months, and the longest period was four years. Four of the patients were exhausted and incapacitated as a result of the prolonged, intense discomfort caused by the disease. Two of the patients had been hospitalized four different times for as long as two to three months at a time, and 2 had been hospitalized at least once. One patient lost approximately 40 pounds (18 Kg.) owing to the various elimination diets that had been prescribed and to restless and sleepless nights. Three of the patients may be considered "cured," and 2 are well except that each has a discoid patch on the glans penis.

REPORT OF CASES

CASE 1.—N. S., a Jewish drygoodsman, born in the United States, had had no previous disease of the skin except urticaria due to acetylsalicylic acid. The personal and family history revealed no record of hay fever, asthma, infantile eczema, atopic dermatitis or other cutaneous disease.

The duration of the present illness was four years. The eruption first appeared on the calves and after a few weeks became generalized. The patient had had, among other remedies, arsenic by mouth, superficial roentgen ray therapy (approximately 600 r) of all affected areas and ultraviolet irradiation, without relief. The condition was diagnosed differently by the various attending dermatologists, "psoriasis?" by some and "eczema?" by others.

I saw the patient for the first time in January 1934. He presented a generalized eruption made up of variously sized and shaped patches of exudative dermatitis. Crusting and scaling were widely distributed over the body, including the face, penis and scrotum. The patient was literally tearing at his skin during the examination because of the intense pruritus. Physical examination gave negative results except for enlargement of the superficial lymph nodes. The blood count was normal except for eosinophilia (6 per cent eosinophils). A histologic examination of one of the cutaneous lesions which had been taken a few months earlier showed a picture suggestive of early mycosis fungoides.

The clinical picture changed completely after one month. The exuding patches healed, and a different type of dermatosis made its appearance. The eruption was now made up of violaceous pea-sized to somewhat larger nodules and infiltrated plaques. The pruritus, however, was just as severe as before. At the time the change in the clinical picture was believed to be due to the use of suitable local remedies, and the nodular lesions were believed to be the primary efflorescence.

Sulzberger and Garbe have pointed out, however, that a change in the clinical picture occurs spontaneously in this disease.

Lymphoblastoma cutis of atypical character was considered as the tentative diagnosis. Because of the clinical resemblance of the condition to lymphoblastoma cutis at this time, daily injections of a 2 per cent solution of sodium arsenate were given, and roentgen therapy was applied to the infiltrated areas.

The initial dose of sodium arsenate was 3 minims (0.18 cc), and the dose was increased by 1 minim (0.06 cc) each day. A shake lotion with 6 per cent ethyl aminobenzoate was prescribed because of the intense itching. The patient began to show signs of improvement two weeks after arsenotherapy was started. When the dose had been increased to 17 drops (1.05 cc) daily, the lesions began to recede. By the time the patient was getting 24 drops (1.5 cc) a day, most of the nodules and infiltrated plaques disappeared, and the lymph nodes were reduced in size. Symptoms of intolerance to arsenic appeared when the dose was increased to 27 minims (1.7 cc). Arsenic was gradually withdrawn by decreasing the dose 1 minim (0.06 cc) each day. A fresh crop of papular lesions accompanied by intense pruritus appeared on the trunk, penis and scrotum when the dose was reduced to 10 minims (0.6 cc). Because of the remission, the arsenic was gradually increased for a second time, to 20 minims (1.2 cc), and again gradually withdrawn.

The aforementioned treatment with arsenic was started Feb. 22, 1934, and the last dose was given May 10. Within three months all signs and symptoms disappeared except for a few nodules on the right shoulder, slightly enlarged lymph nodes and pigmentation in the healed areas. These residua disappeared a few months later, without further treatment. During the time arsenic was administered no area of the skin received more than one erythema dose of roentgen therapy. The patient has been well and free of all signs and symptoms of the disease since October 1934.

CASE 2.—H. E., a Jewish retailer of children's wearing apparel aged 35, born in Russia, had no family or personal history of cutaneous or allergic diseases. Eighteen months prior to his first visit an eruption appeared on the soles, which was so painful that he could not walk. One month later a "crawling" sensation developed on the back, which soon became generalized. The "peculiar sensations" and pruritus gradually grew more intense and in another month were followed by a generalized eruption.

The patient was hospitalized four different times. The shortest stay was five weeks and the longest twelve weeks, but there was little benefit from any of the hospitalizations. Detailed laboratory investigations failed to reveal the cause of the dermatosis. Several biopsies had been performed. The observations were indefinite but seemed to fit in best with the picture seen in early mycosis fungoides. The patient was given numerous injections of calcium, and salves and lotions were applied, without relief. He was also given various elimination diets. No arsenic or roentgen therapy was administered. The patient was totally disabled because of the great loss of weight (40 pounds [18 Kg.]), weakness and long periods of hospitalization.

The patient was first seen in November 1935. He appeared emaciated and extremely weak (height, 6 feet [183 cm.]; weight, 128 pounds [58 Kg.]). A generalized, scaly, pea-sized papular and nodular eruption involved all parts of the body except the genitalia. The superficial lymph nodes were considerably enlarged.

The first impression was that the patient was suffering from lymphatic leukemia or some other form of lymphoblastoma. The blood picture, however, was normal except for eosinophilia (6 per cent eosinophils) and hypochromic anemia, which could be accounted for on a nutritional basis. In view of the resemblance to the first case, the patient began his first course of arsenotherapy on Nov. 20, 1935. One minim (0.06 cc.) of a 2 per cent solution of sodium arsenate was administered hypodermically, and the dose was increased daily by 1 minim. Antipruritic shake lotions and salves were prescribed.

The patient was much more comfortable at the end of two weeks. After the twenty-third dose was administered (23 minims [1.4 cc.]), itching disappeared, the lymph nodes were reduced in size, and the lesions were less infiltrated. At this point roentgen therapy was also started in the hope of hastening resolution of the lesions. Fractional doses of roentgen rays were administered in the usual manner. By the end of the first course of arsenic, which was increased to 54 minims (3.3 cc.), the eruption had cleared up almost completely.

Three weeks later the patient suffered a relapse. Itching appeared first and rapidly increased in intensity. Five days later a generalized maculopapular eruption appeared. A second course of arsenic was started. The first dose administered was half the maximum tolerated dose, 27 minims (1.7 cc.), and the dose was again increased daily. After the administration of 38 minims (2.3 cc.) the lesions began to recede. When a dose of 53 minims (3.3 cc.) per day was reached, all itching had disappeared. Injections were discontinued because of nausea and abdominal pain. A third series of roentgen rays (300 r) was administered to all affected areas during the second course of treatment.

Exactly two weeks after the second course of arsenic therapy was discontinued, new lesions appeared, sparsely distributed at first and then more widespread. This exacerbation, however, did not seem as severe as the previous one. A third course of arsenic therapy was started in the hope of preventing further relapses. The initial dose was 28 minims (1.7 cc.) and was increased in the same manner as previously to 70 minims (4.3 cc.). A fourth series of roentgen rays (300 r) was administered during this course.

Two weeks after the third course, the patient suffered a third relapse, much more severe than the two previous exacerbations, and again became uncomfortable.

Another course of arsenotherapy was considered justifiable in view of the serious nature of the disease (lymphoblastoma picture), the favorable response to previous injections and the absence of ill effects.

The fourth course of arsenotherapy, combined with autohemotherapy, was started July 10, 1936. This course was started with only 1 minim (0.06 cc.), because of the large amounts administered previously, and the dose was increased to 70 minims (4.3 cc.) over a period of seventy days. During this time thirty-two injections of autogenous blood were given in doses of 20 to 30 cc. After the completion of the fourth course, the patient gained weight and had a feeling of well-being. The skin appeared normal except for pigmentation in the previously involved areas. Approximately five or six pea-sized areas of infiltration persisted on the shoulder, abdomen and right flank after the fourth course was discontinued.

In February 1937, five months after the fourth course of arsenic was discontinued, a mild eruption of papular lesions developed on the trunk. The patient was again given injections of a 2 per cent solution of sodium arsenate, starting with 1 minim (0.06 cc.) and increasing to 54 minims (3.3 cc.) At this point arsenic was discontinued, because of neuritic symptoms. At the end of the fifth course, the patient stated the belief that "the turning point had come in his illness" and that he had never felt as well since treatment had been started. Coincidental with the patient's recovery there appeared a tendency for urticarial lesions to develop from time to time, especially when he was excited.

As previously mentioned, the tendency for urticaria to develop when other symptoms of the disease recede was pointed out by Sulzberger and Garbe.

Treatment was discontinued in April 1937, after seventeen months. The skin healed without scarring or atrophy. The patient regained all the weight he had lost, and the blood count returned to normal. He is hale and hearty and is carrying on an active, flourishing business.

CASE 3—L. S., a Jew aged 39, born in Galicia, was a retail grocer before he was incapacitated by his illness. The past personal history and family history were negative for allergy and diseases of the skin.

The popliteal spaces were the first to be involved. After one month the eruption spread rapidly and involved the entire cutaneous surface. The patient had lost 30 pounds (13.6 Kg.) since the beginning of his illness and had been hospitalized on four different occasions. While hospitalized, the patient seemed to improve, only to relapse again soon after he was discharged. He was investigated thoroughly, but nothing pertinent was disclosed. The histologic diagnosis was eczematized dermatitis or irritated psoriasis. There was no evidence of mycosis fungoides.

Numerous injections of calcium and sodium thiosulfate, and approximately thirty roentgen ray treatments to all parts of the body, in addition to the administration of lotions, salves and medicated baths, failed to alleviate the condition.

When the patient was first seen, eighteen months after the onset, the entire integument was involved. The face was studded with split pea-sized bluish red

nodules. The trunk and extremities showed numerous oval and irregular patches of exudation and scaling, as well as ill defined patches of follicular lichenoid papules. Exudative scaly patches were also present on the genitalia. The inguinal nodes were almost egg sized; the axillary nodes were somewhat smaller, and the epitrochlear glands were also definitely enlarged. The patient was too weak to stand during the examination. The blood count was normal except for moderate anemia (69 per cent hemoglobin) and eosinophilia (6 per cent eosinophils).

The clinical resemblance to the first 2 cases was striking. Daily injections of a 2 per cent solution of sodium arsenate were started March 31, 1937 (initial dose 1 minim [0.06 cc.]). During the first two weeks treatment had to be carried out at home. In addition to arsenic, antipruritic shake lotions with ethyl aminobenzoate, a bland diet and an iron preparation were prescribed. Roentgen therapy was not included, because the patient had had approximately thirty treatments, with little benefit.

After two weeks the patient was sufficiently improved to come to the office for treatment. The nodular lesions and infiltrated areas began to recede after the nineteenth dose was administered. The first course of arsenic was discontinued after the twenty-third dose, because a faint trace of albumin was found in the urine. Within three weeks the patient was much more comfortable and had regained 6 pounds (2.7 Kg.). Considerable healing and involution of the lesions had taken place, and the lymph nodes were reduced in size.

Two weeks after the first course of arsenic was discontinued a pale red maculopapular eruption appeared on the neck and trunk. The pruritus also increased. During the first two weeks of the second course, there was no further improvement. New lesions continued to appear in small numbers from time to time until 30 minims (1.85 cc.) was given. From this time on the improvement was striking. The second course was discontinued at 38 minims (2.3 cc.) because of nausea and abdominal pain. At the end of the second course the patient was comfortable. All areas had healed except for three persistent patches of exudation and scaling on the glans penis and a few ill defined patches of follicular papules at the waistline. Urticarial lesions also developed when his condition improved.

Three months after arsenotherapy was started the patient felt well enough to return to work. Except for the penile eruption and evanescent urticarial lesions he appeared to have recovered completely. He gained 10 pounds (4.5 Kg.) during this time, and the hematologic findings returned to normal. Further treatment of the penile eruption over a period of six months, with ultraviolet radiation, roentgen rays and various topical remedies, finally resulted in improvement but failed to clear up the lesions completely.

The patient has been at work since 1937. He is well except for a recurring eczematous eruption of the penis and urticarial lesions which appear from time to time.

CASE 4.—M. L., a Jew aged 35, born in the United States, practiced law before he was incapacitated by his illness.

The family and personal history were irrelevant. The first symptom of the disease was pruritus, followed by a generalized eruption, even on the soles. The condition was diagnosed differently by different observers: dermatophytosis and dermatophytid, lichen planus and, finally, chronic discoid and lichenoid dermatitis. Histologic examinations in two different clinics resulted in diagnoses of contact dermatitis and psoriasisiform type of dermatitis. The patient received various injections and twelve roentgen ray treatments to the

hands and feet. He was hospitalized for ten days, without any appreciable change in his condition. Because of his physical appearance and intense discomfort, he was forced to give up his law practice.

The patient presented a generalized eruption involving the face, trunk and extremities, made up of discoid, oval, violaceous scaly and crusted patches with some tendency to be distributed along the lines of cleavage. Some of the lesions resembled psoriasis and others pityriasis rosea. The scrotal sac was intensely erythematous and scaly. The penis showed crusted, eczematous patches. On the face there were small violaceous nodular scaly lesions. The finger nails and toe nails were thickened and ridged horizontally. The superficial lymph nodes were moderately enlarged, and the pruritus was described as "intolerable." The blood count was normal except for moderate anemia (75 per cent hemoglobin), the eosinophil count was 2 per cent.

Therapy was started on Nov 4, 1938. In addition to daily injections of sodium arsenate, autogenous blood was given every third day, and fractional doses of roentgen rays were administered to previously untreated areas. Combined therapy was decided on in an attempt to reduce the duration of treatment to as short a time as possible. A shake lotion with 6 per cent ethyl aminobenzoate was also prescribed.

After three weeks of the above regimen, the patient was much more comfortable. After five weeks all the lesions had regressed completely except for a few which were still visible on the face. The first course of arsenotherapy was discontinued at 35 minims (22 cc) because of abdominal pain. The only complaint at this time was slight, fleeting pruritus in various parts of the body. Areas of dark brown pigmentation remained to mark the sites of previously affected areas. Thirteen injections of autogenous blood were given, and approximately 450 r of roentgen rays was administered to the affected areas during this time.

Arsenotherapy was resumed after a rest period of two weeks because of the mild pruritus which was still present and because of the infiltrated patches on the cheeks. The second course of sodium arsenate was given over a period of seven weeks. Tolerance had increased to the extent that the patient was able to take 53 minims (33 cc). Early during the second course the pruritus increased somewhat, and during the third week a maculopapular, pale red eruption appeared on the trunk, together with some infiltrated patches on the posterior aspect of the axillary folds. This eruption disappeared again within a few days. With the termination of the second course of treatment the patient was free of itching, the facial lesions cleared up, and the patient felt well enough to resume the practice of law. The only abnormal finding when treatment was discontinued was a sharply defined pea-sized patch of erythema and crusting surrounding the urinary meatus. This lesion has persisted to date. Otherwise, he has been entirely well since Feb 14, 1939.

CASE 5—M B, a Jewish clothes operator aged 54, born in Russia, had intense itching of all parts of the body and a generalized eruption of eighteen months' duration.

The family and personal history were irrelevant.

The eruption first appeared on the soles and shortly after became generalized, even on the face and genitalia. The patient was hospitalized during the first month of his illness. Urine, blood tests and cutaneous tests gave negative results. Treatment included injections of calcium gluconate, fever therapy, application of various unguents and lotions and approximately six roentgen ray treatments of all affected parts. The condition seemed to be getting progressively worse, but the patient was able to continue working.

The clinical picture was almost identical with that in case 4. A histologic examination made six months previously was reported as "chronic eczema." The blood count was normal except for 8 per cent eosinophils.

On Oct. 12, 1939, the patient began a combined course of arsenotherapy, injections of autogenous blood and superficial roentgen ray therapy. A few areas were screened off from the rays in order to compare the progress of these lesions



Fig. 1 (case 5).—Nodular and infiltrated scaly plaquelike lesions before treatment was begun.

with those exposed to radiation. A shake lotion containing 6 per cent ethyl aminobenzoate was also prescribed. After the tenth dose of solution of sodium arsenate was administered, the patches in the cubital fossae began to regress. When a daily dose of 17 minims (1.05 cc.) was reached, definite regression in all patches had appeared. The pruritus began to abate but was still considerable. The first course of arsenic was discontinued at 33 minims (2 cc.). By this time the patient was comfortable, and the eruption had cleared up, leaving areas of dark brown pigmentation and patches of scaling on the lower extremities. Eleven

injections of blood were given, and not more than 225 r of roentgen rays had been given to any area up to the time definite signs of improvement began. The areas shielded from the roentgen rays improved but not as rapidly as the irradiated areas.

On November 25 a second course of arsenotherapy was started to prevent the possibility of a relapse. The injections were administered over a period of six weeks and the maximum dose was 45 minims (2.8 cc). By the end of the second course all lesions had disappeared except for a few split pea-sized papules below the eyes. A total of 450 r had been administered to the affected areas. The

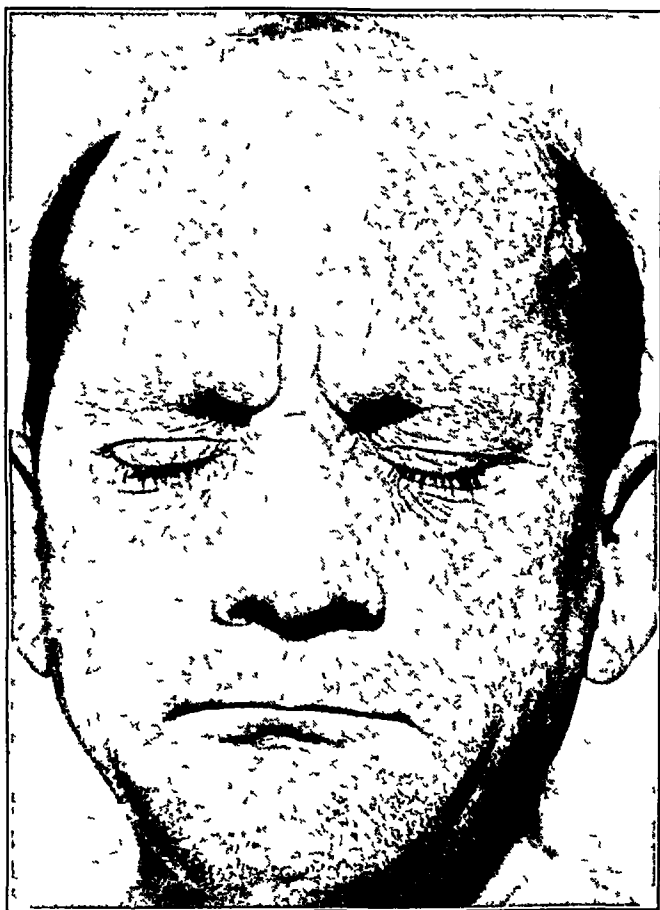


Fig 2 (case 5)—All lesions are completely healed after three months of treatment

persistence of the lesions near the eyelids was attributed to the fact that this area had received only one-half the amount of roentgen rays given to the rest of the face. With an additional 150 r these lesions disappeared as well.

Treatment was discontinued Jan 8, 1940. There have been no signs or symptoms of a relapse since treatment was started.

COMMENT

Five cases of "exudative chronic lichenoid and discoid dermatitis" (Sulzberger and Garbe) have been described. A new approach to treatment was made, which proved highly successful in these patients.

The essential feature of this treatment was repeated courses of subcutaneous injections of a 2 per cent solution of sodium arsenate. At least two such courses were required, and in 1 case as many as five courses were found to be necessary. The first course was started with a subcutaneous injection of 1 minim (0.06 cc.) of solution of sodium arsenate. Injections were given daily, the dose being increased by 1 minim each time. The course of treatment was stopped when the patient began to complain of nausea, vomiting, abdominal pain, diarrhea or numbness and tingling of the extremities or if albumin appeared in the urine. One of the symptoms of intolerance usually appeared when the daily dose had been raised to approximately 30 minims (1.85 cc.). After a rest period of about two weeks a second course was started. A decided increase in tolerance to the drug was found during the second course, the patient frequently being able to tolerate as much as 53 minims (3.1 cc.) a day. The average total dose given was 500 minims (30.8 cc.) during the first course and 800 minims (49.2 cc.) during the second course. Exsiccated sodium arsenate N. F. was used in preparing the solution ($\text{Na}_2\text{HAsO}_4 \cdot 7\text{H}_2\text{O}$). This means that the average total dose of metallic arsenic was 0.142 Gm. in the first course and 0.23 Gm. in the second course.

The parenteral method of treatment was adopted rather than the oral administration of solution of potassium arsenite, U. S. P., because the latter had been tried and had failed in the first case. Failure with the oral method had been noted in a case similar to the first case by Rostenberg.⁵ The parenteral method may actually be superior to the oral method, because a much greater tolerance for the drug seems to develop when it is administered in this way, and, furthermore, one does not have to depend on the patient's cooperation. On the other hand, had the oral administration of arsenic been persisted in, the effects might have proved equally beneficial.

In addition to arsenic, these patients received autohemotherapy and roentgen therapy. It is my impression that roentgen therapy and autohemotherapy are beneficial but of secondary importance. Treatment with roentgen rays alone has been tried by others in similar cases,⁶ without success. One patient, case 3, received a considerable amount of roentgen therapy elsewhere without benefit, and then improved rapidly when roentgen ray therapy was stopped and the administration of arsenic was begun. Finally, in each case resolution of the lesions together with symptomatic improvement began within three weeks after arsenotherapy

5. Rostenberg, A., and Rostenberg, A., Jr.: A Case for Diagnosis, *Arch. Dermat. & Syph.* **35**:509 (March.) 1937.

6. Bechet, P. E.: A Case for Diagnosis (Eczematoid Dermatitis? Mycosis Fungoides?), *Arch. Dermat. & Syph.* **30**:165 (July) 1934.

was started. The 150 or 225 r given during this time in some of the cases could hardly account for the rapid improvement.

All the patients were kept on a high caloric bland diet. Iron was prescribed when necessary. I found that a shake lotion or ointment with ethyl aminobenzoate frequently gave needed relief during the early days of treatment. These 5 patients have now been well for between one month and six years. There has been no recurrence in any case. Two of the patients still have a patch of dermatitis on the penis, which has persisted throughout the entire period of treatment. Four were entirely disabled before treatment was begun, but they all now enjoy good health and have been able to resume their occupations.

Note should be taken of the fact that these patients were treated at home, without changing their normal environment or mode of living.

The cause, pathogenesis and proper nosology of this dermatosis are still to be determined. The observations made, however, help to clarify one or two points. A sensitization or allergic mechanism has been considered as a possible explanation of the *modus operandi*, despite the fact that in most cases cutaneous tests, family and personal history were negative for allergy. This hypothesis was based on the observation that most patients suffering from the disease responded well to a complete change in environment, only to relapse on returning to their usual surroundings. The fact that these patients can be treated successfully without changing their normal environment or mode of living would seem to be against the aforementioned theory.

In each of the 5 cases the clinical picture was suggestive of lymphoblastoma cutis because of the intense pruritus and nodular and infiltrated plaque-like lesions. The argument that this dermatitis cannot be classified among the cutaneous lymphoblastomas because the eruption fails to respond to arsenic and roentgen therapy can now be overruled. Objections to such classification must rest on the atypical clinical features and the lack of histologic evidence to support such a contention.

SUMMARY AND CONCLUSIONS

Five cases are presented in which the characteristics, course and other findings were closely parallel to the syndrome described by Rosen and by Sulzberger and Garbe.

The patients were treated by subcutaneous injections of a 2 per cent solution of sodium arsenate, superficial roentgen ray therapy and auto-hemotherapy.

The evidence suggests that the most effective factor of this combined therapy was the arsenic.

The treatment described was successful in 5 consecutive cases.

INJURIES OF THE MOUTH CAUSED BY THE TEETH

DOUGLASS W. MONTGOMERY, M.D.

SAN FRANCISCO

In a case of erosion of the tongue or of the lining of the lips or cheeks one naturally looks for roughness or inequalities of the teeth. According to Bangai,¹ however, who has reported 2 cases, such a condition may be caused by pressure alone on perfectly smooth teeth; he mentioned also that if a tooth is lost the tongue, pressing into the inequality, may cause an erosion. This is especially true of the papillae foliatae (perpendicular folds) on the sides of the tongue just in front of the anterior pillars of the fauces, mentioned by Greenbaum² as subject to irritation from irregular teeth.

A patient of mine was much worried, and rightfully so, because of an enduring inflammation and swelling in this locality. The teeth of her denture were slightly tipped inward, but they were smooth and well set. Her dentist ascribed her trouble to the tongue being too large, for some unknown reason, for the mouth. With the use of an abundance of elm-boric acid mouth wash the trouble subsided.

An ordinary canker sore, an aphtha, may become irritated by an otherwise inoffensive tooth and cause an erosion, enduring, uncomfortable and mentally disturbing. I have seen examples of this which persisted after all dental inequalities had been cared for. Healing can be secured by wearing a piece of chewing gum over the teeth in this location, thus keeping the mucous membrane entirely away from the teeth. This is better than a piece of gauze, the remedy sometimes advised, as it is smooth, solid and yet plastic and fits well against the teeth.

Erosions may be grave, as in a woman, the subject of the photograph, who was 58 years of age but looked much older. Also of interest is the fact that she had had an epithelioma of the right temple which had yielded to treatment.

The erosion was a pincushion-like lesion, with a yellow surface, $\frac{3}{8}$ inch (0.95 cm.) in diameter, situated on the inner surface of the lower lip well within the mouth and directly where the long sharp fang of

1. F. Zinsser (Hautkrankheiten und Mundschleimhaut, in Jadassohn, J.: *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1930, vol. 14, pt. 1, p. 74) quoted Bangai as mentioning the occurrence of lesions due to the tongue pressing against perfectly normal teeth.

2. Greenbaum, S. S.: Glossodynia and the Painful Form of Wandering Rash of the Tongue, *Arch. Dermat. & Syph.* **39**:686 (April) 1939.

one of the upper lateral incisors dug into it. The tissue inclinations of the patient, as indicated by their obvious senility and by the occurrence of an epithelioma, together with the physical appearance of the lesion itself, aroused definite suspicion of malignancy. The elimination of the offending tooth, however, resolved the trouble favorably.

TRAUMATISMS OF THE BORDER AND TIP OF THE TONGUE

Traumatism of the border and of the tip of the tongue have a decided inclination to become indurated and therefore to simulate in



Pincushion-like erosion of mucous membrane surface of lower lip in a situation where the long sharp fang of an upper incisor tooth dug into it. The teeth and gums were in extremely bad condition. The skin of the face shows senile changes.

this important respect infiltrative diseases like cancer, syphilis and tuberculosis. This inclination in this situation is due to the connective tissues here having a perpendicular set and the blood vessels a fanlike distribution, so favoring deep infiltration by these diseases.

As a striking example of this, a man aged 53 consulted me on Sept. 8, 1924, for a lesion on the right border of the tongue directly opposite the right lower premolar. The upper premolar had a sharp inner edge. Pain was acute and radiating. The appearance was so suspicious that I made a tentative diagnosis of epithelioma, although

the patient said that the condition had begun only two weeks previously as a crack. It cleared up after rectification of the dental condition and the use of a simple mouth wash.

Even an acute recent traumatism of this locality may exhibit the peculiarity of excessive induration to a striking extent, as shown in the case of a man, aged 78 but enjoying excellent health, who while the mucous membranes of the mouth were swollen by a "cold" bit the left border of his tongue midway between the tip and the base, causing intense pain. The wound bled for several hours, causing clots, which he spat out. The following day a physician on viewing the lesion thought it was a tumor, and if it had been this naturally would have explained its having been bitten.

The cakelike lesion was about $\frac{1}{4}$ inch (0.6 cm.) in diameter and was prominent and accurately circular and in its center had a slitlike wound. Its upper border flattened off into the dorsum of the tongue, but the lower border was thicker and ended in a rolled edge overhanging the border of the tongue. It was tender and was decidedly indurated. A dentist rounded off the edges of the opposing teeth, some of which had grown to be rather sharp. Gradually the tenderness and the induration subsided, so that twenty-four days afterward the area appeared slightly sunken and covered with white imperfect epithelium, with the wound still visible in its center. Less than a month afterward the lesion had healed, leaving no trace either visibly or subjectively.

Here may be mentioned a happy circumstance connected with wounds of the mouth. Even large wounds in this cavity heal kindly, leaving little or no trace. This is attributed to the warmth and moisture of the mouth, and it may be that the oral juices, if not directly antiseptic, are unfavorable to the growth of the pathogenic microorganisms.

Lesions of the dorsum of the tongue may be deeply indurated, but the tendency is not nearly so great as on the borders. This condition was well exemplified in the case of a man aged 54 who consulted me on Jan. 6, 1926, for an uncomfortable feeling of the dorsum of the tongue near the right border. The only local symptom was a semicircular line of deep indentations. This, however, was opposite a tooth with a rough mammillated crown, which beat down directly on this surface. Attention to this tooth cleared up the condition. The patient had a sensitive mouth subject to simple herpes, for an attack of which he subsequently consulted me.

Some of these wounds are severe, such as those received in an epileptic fit, during which the tongue may be violently protruded and the spasm may then clamp the teeth firmly on it, inflicting a grave wound or even biting off the tip. The wound, however, heals kindly,

and even if the tip is bitten off it may be sewed on, with the area under local anesthesia, during the hebetude following the fit³

An ulcer may also occur on the under surface of the tongue and on the frenulum caused by the protruded tongue striking against the lower front teeth in the violent coughing of whooping cough

In these irritable lesions the mouth wash prescribed is important. It should be so inexpensive that it may be used abundantly and should be mildly antiseptic and suave. The following preparation, with which I first became acquainted through the late Louis Brocq, of Paris, France, meets these requirements

Place a bunch of elm N F in a pint (473 cc) jar which has been scalded. Pour over this enough boiling water to fill the jar. Let steep for twenty minutes and then strain by pouring through clean cloth or gauze. Then add 2 heaping teaspoonfuls of boric acid powder. Keep in covered jar or in a bottle. Carry a small bottle of the mouth wash and gargle with it several times a day.

CONCLUSIONS

The teeth of the mammals, especially of the carnivora, among which human beings are included, are stout instruments meant to tear and grind food and also to be weapons of attack and defense. The soft delicate mucous membranes of the lips and cheeks lie against the outer surfaces of these formidable instruments, and the cheeks have an 'inter-dental line,' often projecting inward along the outline of the bite. In like manner the tongue with its rounded borders lies along the inner line of the bite, and not infrequently it is so swollen and soft and lies so closely against the teeth that it takes their impression, causing what is called "orchestria chair tongue."

One would think, from the apparent imminence of the danger, that accidental biting of the cheeks or tongue would be frequent, yet its occurrence is rare. Nature provides against such an accident.

In estimating such an injury one must always bear in mind that it may be not a simple erosion but a syphilitic, tuberculous or cancerous lesion in its incipency, bitten because of its protrusion.

³ Spencer, W. G., and Cade S. *Diseases of the Tongue*, Philadelphia, P. Blakiston's Son & Co., 1931, p. 59.

NEUROFIBROMATOSIS ASSOCIATED WITH CARCINOMA OF THE BREAST AND PREGNANCY

HERMAN CHARACHE, M.D.
BROOKLYN

Although neurofibromatosis associated with pregnancy has been reported in a few instances,¹ the association of multiple neurofibromas with carcinoma of the breast and pregnancy has not been previously reported.

The influence of pregnancy on the growth of malignant tissues has been observed by a number of clinicians. This phenomenon has also been noted concerning neurofibromas, with increase in size and number of the tumors. The pigmentation becomes more evident, and pain becomes a more predominant symptom. The latter is the result of pressure on the cutaneous nerve filaments by the increase in size and number of the tumors. When pregnancy is terminated, there is a regression in the size and number of the nodules. In the case reported by McNally² the cutaneous lesions had subsided about 40 per cent eight months after the termination of pregnancy.

When pregnancy again supervenes, the process repeats itself. This is illustrated by a case reported by Nishizaki.^{1c} The offspring in a great number of cases is subject to the same disease, either in childhood or later in life. It is now generally agreed that heredity is a predisposing factor in neurofibromatosis.

A search through the literature fails to reveal any reports of neurofibromatosis associated with carcinoma of the breast, although Davis, Hanelin and Mouzakeotis³ reported a case of carcinoma of the male breast associated with a neurofibromatous nodule of the back and a tumor of the thigh of myogenic origin.

From the Brooklyn Cancer Institute.

1. (a) Sutton, R. L.: *Am. J. M. Sc.* **147**:419, 1914. (b) Hirsch, E.: *Med. Klin.* **23**:983, 1927. (c) Nishizaki, S.: *Jap. J. Obst. & Gynec.* **11**:241, 1928. (d) Kushner, J. I.: *Am. J. Obst. & Gynec.* **21**:116, 1931. (e) Sharpe, J. C., and Young, R. H.: *Neurofibromatosis: Effect of Pregnancy on Skin Manifestations*, *J. A. M. A.* **106**:682 (Feb. 29) 1936.
2. McNally, H. B.: *Am. J. Obst. & Gynec.* **33**:501, 1937.
3. Davis, G. G.; Hanelin, H. A., and Mouzakeotis, T. C.: *Multiple Tumor Syndrome in Male: Carcinoma of Breast, Pleomorphic Sarcoma of Thigh and Neurofibromas of Skin; Report of Case*, *J. A. M. A.* **106**:1359 (April 18) 1936.

REPORT OF A CASE

A white woman aged 30 was admitted to the Brooklyn Cancer Institute on Dec 9, 1925, with a diagnosis of multiple neurofibromas and a malignant condition. The patient complained of inability to walk due to pain in both knees and back.



Fig 1—Photomicrograph ($\times 200$) showing carcinoma of the breast in a case of neurofibromatosis

She also had pain in the right side of the chest, right axilla and right arm. The pain in the chest was aggravated by a cough of six weeks' duration.

At the age of 14 she noticed multiple nodules over her body. As she grew older the nodules increased in number, but they never gave her any discomfort.

At the age of 17 she had her first menstrual period; the periods were always regular and lasted four days. She married at the age of 23 and had three pregnancies, with the birth of one living child. At the time of the patient's admission, her child was 5 years of age, and in good health. The other two pregnancies ended in miscarriages, one at five months and one at seven and one-half months. At the time of admission she had not menstruated for three months.

In 1924 she noticed a tumor in her right breast. She was admitted to a hospital, where a diagnosis of carcinoma of the breast was made and a radical mastectomy was performed. The diagnosis was confirmed by histologic examination of the tissue of the breast (fig. 1). On examination of the slide at the Brooklyn Cancer Institute, the diagnosis was again confirmed. The glands in the axilla proved to be metastatic, but one of the numerous nodules on her chest, removed for examination, proved histologically to be fibromatous in origin. There was no record of multiple neurofibromas or a related condition in members of this woman's family, nor was the cause of her parents' death of any significance.

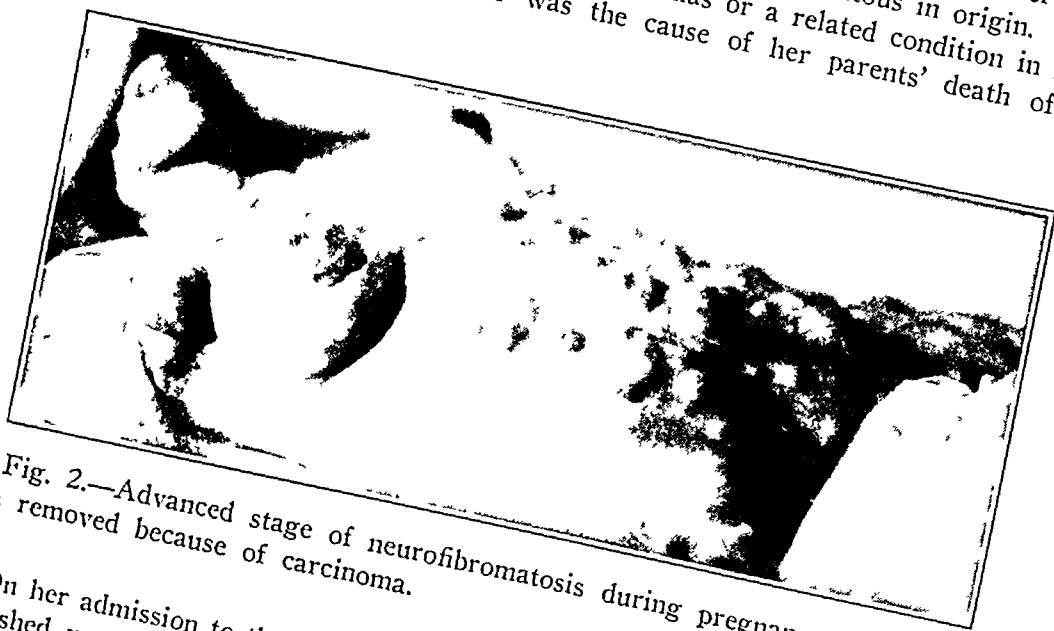


Fig. 2.—Advanced stage of neurofibromatosis during pregnancy. Left breast was removed because of carcinoma.

On her admission to the hospital, examination revealed a chronically ill, poorly nourished woman, with hippocratic facies, temperature 97 F., pulse rate 150 and respiratory rate 24. The entire body, including the extremities, was covered with numerous nodules, varying from 1 to 3 cm. in size. There was little intervening normal skin. The patient appeared like a museum specimen composed of multiple nodules (fig. 2). The right breast was missing. A scar measuring 12 inches (30.5 cm.) in length was visible. The left breast was covered with subcutaneous nodules, but there was no tumor palpable within the breast. Harsh bronchovesicular breathing, with occasional whistling expiratory rales, was heard over both lungs. The heart sounds were of good quality, and no murmurs were heard.

The abdomen was scaphoid, with little subcutaneous tissue. The liver and spleen were not palpable. With the exception of the subcutaneous nodules, there were no other tumors palpable. Pelvic examination revealed the cervix to be soft. The fundus was enlarged to the size of a three month pregnancy and was soft. The fornices were free from any palpable tumefaction.

With the exception of the multiple nodules, the extremities did not show any clinical abnormalities

The urine was normal The Wassermann reaction of the blood was negative Chemical examination of the blood showed urea 28 mg, creatinine 0.96 mg and sugar 65 mg per hundred cubic centimeters

The final clinical diagnosis was (a) multiple neurofibroma, (b) carcinoma of the breast, with metastasis to the lungs, and (c) pregnancy

The patient remained in the hospital for supportive treatment and died on Jan 21, 1926 Permission for autopsy was not obtained

75 Prospect Park Southwest

Clinical Notes

SULFAPYRIDINE DERMATITIS

Report of Two Cases

C. G. LARocco, M.D., CLEVELAND

The advent of any new drug creates the necessity of being alert to a complicating eruption.

While the possibility of a sulfanilamide eruption is well known, I have found only casual reference in the American literature to dermatitis caused by sulfapyridine. Therefore, the following report is made.

REPORT OF CASES

CASE 1.—T. L., a white boy aged 13, was admitted to the medical service of Dr. Edward W. Parsons at St. Vincent Charity Hospital on Feb. 5, 1940, because of a cold and cough. Six days later a diagnosis of pneumonia was made (no specific type), at which time sulfapyridine was ordered, 15 grains (1 Gm.) every four hours. On February 18, one week after administration of the drug, a morbilliform eruption appeared. This rash was generalized, symmetric and macular. On the face and trunk it was almost solid and there was dusky erythema, while on the abdomen and extremities the macules were arranged in circles and crescents. The conjunctivas and buccal mucosae were clear.

On admission the blood count showed: erythrocytes, 5,000,000 per cubic millimeter; hemoglobin, not reported and leukocytes, 22,000 per cubic millimeter, with the differential count polymorphonuclear neutrophils 64 per cent, small lymphocytes 16 per cent, monocytes 10 per cent and large lymphocytes 10 per cent. On February 12, the erythrocytes had dropped to 3,600,000 per cubic millimeter and the leukocytes had increased to 32,000 per cubic millimeter. On February 19 the erythrocytes were 3,800,000 and the leukocytes 18,000 per cubic millimeter, while the differential count showed polymorphonuclear neutrophils 63 per cent, small lymphocytes 12 per cent, monocytes 5 per cent and large lymphocytes 20 per cent. On February 23 the erythrocytes were 3,900,000 and the leukocytes 11,000 per cubic millimeter.

CASE 2.—M. E., a white woman aged 25, was admitted to the service of Dr. John P. Anderson at St. Vincent Charity Hospital on May 14, 1940, with a diagnosis of lobar pneumonia of type I. On that day she received 100,000 units of type I antipneumococcus serum and was given 30 grains (2 Gm.) of sulfapyridine at once and then 15 grains (1 Gm.) every four hours. On May 22, eight days after administration of this drug, a rash was noted. The face was flushed and mildly cyanotic. On the trunk the eruption was morbilliform, flat and pink. On the abdomen it was confluent, fading onto the thighs. The lesions were devoid of the edematous character commonly observed with rubeola and of the urticarial phenomena of serum sickness. The conjunctivas and buccal mucosae were clear.

From the Dermatological Service of Dr. Clyde L. Cummer and Dr. C. G. LaRocco, at St. Vincent Charity Hospital.

Twenty-four hours after the administration of this drug was interrupted in both cases the rash had practically disappeared, and in less than forty-eight hours the skin was entirely clear. The character and ephemeral course of the eruption correspond with the reports of Davis¹ and Rosenfeld and Rosenblum².

The hemogram in case 2 closely resembled the blood picture in case 1. Repeated urinalyses in both cases showed no albumin or sugar.

1 Davis, E. Dermatitis and Stomatitis in Pneumonia Treated with M & B 693 (Sulfapyridine), *Lancet* **1** 1042 (May 6) 1939.

2 Rosenfeld, J., and Rosenblum, A. Sulfapyridine in the Treatment of Pneumonia. Observations in One Hundred Cases, *Ohio State M J* **36** 385-388 (April) 1940.

News and Comment

A STUDY TO EVALUATE ORIGINAL SEROLOGIC TESTS FOR SYPHILIS

More than five years ago the Committee on Evaluation of Serodiagnostic Tests for Syphilis, in cooperation with the United States Public Health Service, conducted a study to evaluate original serologic tests for syphilis or modifications thereof in the United States. The results of this study were published shortly after the investigation was completed (Cumming, H. S.; Hazen, H. H.; Sanford, A. H.; Senear, F. E.; Simpson, W. M., and Vonderlehr, R. A.: The Evaluation of Serodiagnostic Tests for Syphilis in the United States: Report of Results, *Ven. Dis. Inform.* **16**:189 [June] 1935; The Evaluation of Serodiagnostic Tests for Syphilis in the United States, *J. A. M. A.* **104**:2083 [June 8] 1935).

Consideration is now being given by the committee to the organization of a second evaluation study of original serologic tests for syphilis or modifications thereof within the next year. If the need for an investigation of this kind seems to justify the cost, invitations will be extended to the authors of such serologic tests who reside in the United States or who may be able to participate by the designation of a serologist who will represent them in this country. The second study will be conducted utilizing methods comparable to those employed in the first study (Cumming, H. S.; Hazen, H. H.; Sanford, A. H.; Senear, F. E.; Simpson, W. M., and Vonderlehr, R. A.: The Evaluation of Serodiagnostic Tests for Syphilis in the United States, *J. A. M. A.* **103**:1705 [Dec. 1] 1934).

Serologists who have an original serologic test for syphilis or an original modification of a test and who desire to participate in the second study should submit their applications not later than Oct. 1, 1940. The applications must be accompanied by a complete description of the technic. All correspondence should be directed to the Surgeon General, United States Public Health Service, Washington, D. C.

EXAMINATION FOR CERTIFICATION BY THE AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

A written examination will be held in various large cities in the country on Monday, Oct. 28, 1940. Applications must be received by the secretary by September 16. An oral examination will be held in Chicago on Friday and Saturday, December 6 and 7. Applications for group A candidates must be received by November 1 by the secretary, Dr. C. Guy Lane, 416 Marlboro Street, Boston.

Abstracts from Current Literature

EDITED BY DR HERBERT RATTNER

THE EXANTHEM OF ACUTE MONONUCLEOSIS H J TEMPLETON and R T SUTHERLAND, J A M A **113** 1215 (Sept 23) 1939

The hospital records of the students at the University of California were studied by Templeton and Sutherland, who found records of 91 cases of acute mononucleosis. There was an associated eruption present in 17 of these patients (18.5 per cent), which was usually indistinguishable from rubella. Rarely the rash was erythematous or consisted of multiform lesions. Itching was mild or absent. The eruption was noted at various times during the course of the disease, appearing anywhere from the third to the twentieth day. The duration was from three to seven days.

CORNEAL EXAMINATION AND SLIT LAMP MICROSCOPY IN DIAGNOSIS OF LATE CONGENITAL SYPHILIS, ESPECIALLY IN ADULTS J V KLAUDER and A COWAN, J A M A **113** 1624 (Oct 28) 1939

According to the experiences of Klauder and Cowan, the type of interstitial keratitis caused by syphilis can usually be differentiated from other forms, when the cornea is studied by means of slit lamp microscopy. This method may also be the only means of detecting the disease when substantial recovery has occurred. They studied 100 patients with interstitial keratitis, ranging in age from 6 years to 65, the majority being under 30. They concluded that slit lamp microscopy is more reliable in the diagnosis of old interstitial keratitis than is study by oblique illumination and the ophthalmoscope. Klauder and Cowan stress the importance of the diagnosis of old interstitial keratitis as valid evidence of congenital syphilis and point out that the differentiation between congenital and acquired syphilis is of importance in the therapy to be administered.

SEROLOGIC DISCREPANCIES IN SYPHILIS G M CRAWFORD and L F RAY, J A M A **113** 1715 (Nov 4) 1939

Crawford and Ray found that of 2,862 new patients admitted to the syphilis clinic at the Massachusetts General Hospital in a two year period, 335 with late stages of the disease showed a positive Hinton and a negative Wassermann reaction. Of the 335 patients whose serologic tests were at variance, nearly 50 per cent were found by subsequent study to have syphilis, and 25 per cent more were presumed to have syphilis solely because the Hinton test gave a persistently positive reaction. Of the remaining 25 per cent, the status of half was not determined, while in the other half the initial positive reaction was considered to be due to a technical error. Crawford and Ray found the Hinton test to possess a high degree of specificity and obtained only 0.42 per cent false positive reactions in the reported series of cases.

A CLINICAL STUDY OF ACNE IN UNIVERSITY STUDENTS F W LYNCH, J A M A **113** 1792 (Nov 11) 1939

Lynch studied three large groups of both boys and girls with acne in the freshman class at the University of Minnesota. The median age of the boys was 19 and of the girls 18. The incidence of acne was determined to be 57 per cent for the boys and 46 per cent for the girls. The severe pustular forms and involvement of the trunk were more commonly found among the boys. There

was no determined relation between the presence of acne and the body build or body weight. It was noted, however, that asthenic girls were unlikely to suffer from the severe forms of acne. There was an apparent trend to an increased basal metabolic rate in the more severe cases of acne in both sexes. According to Lynch, the statement of the patient regarding the character of the menses is usually not dependable. When this question was carefully checked, there was an apparent incidence of abnormal menses in about 40 per cent. There was no relation between the texture or the color of the hair and the presence of acne. Seborrhea was common and more often noted with the severe forms. Girls without acne wash less frequently, probably because of lack of need of attention. The incidence of constipation was negligible. Focal infection of the nose or throat was more common in boys than in girls. A series of 49 girls with acne was treated by Lynch by the application of the dihydroform of estrogen. Improvement was noted in 72 per cent of those treated, but in 64 per cent of a control series, in which the base alone was used, there was a similar improvement.

THE USE OF COLLOIDAL CALOMEL (MILD MERCUROUS CHLORIDE) OINTMENT IN DERMATOLOGY. T. CORNBLEET, A. H. SLEPYAN and M. H. EBERT, J. A. M. A. **113**:1804 (Nov. 11) 1939.

Cornbleet, Slepian and Ebert studied the clinical effect of a colloidal mild mercurous chloride ointment (calomel) in a variety of dermatologic conditions. Its chief use was found to be in the treatment of impetigo contagiosa and certain of the superficial pyodermas, but it was also effective when applied to the form of seborrheic eczema localized behind the ear and also to infected ulcers of the leg.

CONTACT DERMATITIS DUE TO MANGO. S. J. ZAKON, J. A. M. A. **113**:1808 (Nov. 11) 1939.

Zakon reports 2 instances of sensitivity to the peel of the mango. The diagnosis was proved by patch tests. In both cases there was considerable edema and a vesicular eruption of the lips and circumoral tissues. Zakon points out that the mango and *Rhus toxicodendron* both belong to the family Anacardiaceae and that in his 2 cases the appearance of the rash was comparable to that produced by *Rhus*.

MAPHARSEN IN TREATMENT OF SYPHILIS IN OFFICE PRACTICE: A STUDY BASED ON TWO THOUSAND, THREE HUNDRED AND FORTY-TWO INJECTIONS OF ONE HUNDRED AND THIRTEEN PATIENTS. C. R. REIN and F. WISE, J. A. M. A. **113**:1946 (Nov. 25) 1939.

According to Rein and Wise, mapharsen is an acceptable arsenical preparation for use in office practice. They found mapharsen to be relatively nontoxic, and few untoward reactions occurred. In 1 instance, despite the daily administration of conventional doses, it was not effective when unsupported by a heavy metal. The best method of administration was found to be by concurrently giving a preparation of heavy metal. They report a fatality in a woman aged 30, in whom aplastic anemia developed during the second course of administration of mapharsen. This is the first recorded case of the development of a blood dyscrasia with a fatal outcome following the use of mapharsen.

CONTACT DERMATITIS FROM OPIUM DERIVATIVES WITH SPECIAL REFERENCE TO OCCUPATIONAL ASPECTS. J. W. JORDON and E. D. OSBORNE, J. A. M. A. **113**:1955 (Nov. 25) 1939.

The cutaneous reactions which may occur after the ingestion of opium or its derivatives are well known. Jordon and Osborne report cutaneous sensitivity from contact with these substances in 4 patients. Three of the patients were nurses,

and the fourth was a medicinal tablet molder. Confirmation was obtained by patch tests. In 1 instance an extreme degree of sensitization was noted, a patch test with a dilution of 1 1,000,000 producing a strongly positive reaction.

SEVERE ALLERGIC DERMATITIS FOLLOWING THE PARENTERAL USE OF THEELIN [ESTRONE] L A LEVISON and J J HARRISON, *J A M A* **113** 2055 (Dec 2) 1939

A woman, aged 51, received eight injections of one brand and one injection of another brand of an estrogen, estrone (theelin) N N R. After each injection local pain and itching were present. After the fourth or fifth injection an eruption developed near the sites of the injections. The rash progressed in severity and finally became generalized. The affected skin showed erythema and vesiculation. Edema was present around the ankles. Intradermal tests revealed a sensitivity to both peanut oil and cottonseed oil, and the cutaneous efflorescence was considered due to allergy to these oils and not to the estrogen in the preparations.

SOBISMINOL MASS. CLINICAL RESULTS WITH ORAL ADMINISTRATION J R SCHOLTZ, K D McEACHERN and C WOOD, *J A M A* **113** 2219 (Dec 16) 1939

Scholtz, McEachern and Wood report on the treatment by sobisminol mass (orally) of 90 patients with various types of syphilis. At first they prescribed nine capsules, which represented 1.25 Gm of bismuth, but a dose of 0.84 Gm was later determined to be optimal. They found no evidence of cumulative toxic effects and concluded that no depots were formed. The complications were frequent (50 per cent of all patients) but mild. Only 4 patients were unable to continue treatment, while 7 others stopped for from one to two weeks and were then able to resume. Nausea and vomiting were the commonest complaints. A few patients had a bismuth line, stomatitis, a "grip syndrome," urinary frequency, ptialism or parotitis. Two patients had esophageal spasm, due, it was thought, to the dissolving of the capsule in the lower end of the esophagus, with subsequent erosion of the mucous membrane. Sobisminol mass was found to be effective in bringing about involution of active syphilitic lesions of the skin. It is a preferred method of treatment to bring relief from the symptoms of late neurosyphilis (particularly the tabetic form).

FATALITY RATES IN THE TREATMENT OF NINE HUNDRED AND NINETY-EIGHT ERYSIPELAS PATIENTS. THE INFLUENCE OF SULFANILAMIDE A L HOYNE, A A WOLF and L PRIM, *J A M A* **113** 2279 (Dec 23) 1939

In an analysis of 998 patients with erysipelas cared for in the contagious disease department of the Cook County Hospital during the years 1929 to 1938, inclusive, Hoyne, Wolf and Prim report a reduction in the mortality rate from 17.3 per cent in the first year of the decennium to 2.1 per cent in the last year. The authors consider that the use of sulfanilamide is chiefly responsible for the lowered mortality rate and is the most effective form of therapy yet used in the treatment of erysipelas. Sixty per cent of the patients were males, and the fatality rate for males was almost exactly double the corresponding rate for females. The disease was observed most frequently in the spring and winter, particularly in March and April. Bronchopneumonia was the most important complication causing death, while patients with organic heart disease were found to be unusually poor risks when subjected to attacks of erysipelas.

Lewis, New York

KERATODERMA BLENNORRHAGICUM. H. SEDDON TAYLOR, Brit. J. Dermat. **51**: 418 (Oct.) 1939.

Taylor reports excellent results in 3 cases by treatment with hyperpyrexia, induced by means of the Kettering hypertherm, and with the application of "elastoplast" to the lesions. The elastoplast is kept on until "semi-liquid, evil-smelling debris begins to ooze through." A study of the literature leaves no doubt that the disease is a definite clinical entity, a manifestation of gonorrhea, but there is some question as to whether it is toxic, metastatic, septic or allergic in origin. Taylor believes it to be a part of a septicemic process.

PATHOGENESIS OF KERATOSIS BLENNORRHAGICA. ERVIN EPSTEIN, Brit. J. Dermat. **51**:428 (Oct.) 1939.

Epstein calls attention to: (1) the infrequency and inconclusiveness of the reports of cases in which the gonococcus was found in the cutaneous lesions; (2) the appearance of crops of lesions on widely separated, usually bilateral areas of the body at one time (the blood cultures are sterile, and lesions have been seen on mucous membranes of the mouth); (3) the coexistence in some cases of toxic manifestations in the eye; (4) the predilection for the palms and soles, sites usually involved by the commonest of ids, the dermatophytid; (5) the response of the cutaneous lesions to cure of the primary focus and the inefficacy of local therapy, and (6) the positive reaction to the complement fixation test in some 70 per cent of the cases and the appearance of urethritis and arthritis prior to the development of the keratosis, which occurs usually with relapse of the former.

For these reasons Epstein holds that the cutaneous lesions represent an idiosyncratic immunologic response of a previously prepared tissue to the stimulus furnished by the interaction of the gonococcus with its environment in the lower part of the urogenital tract and in the articular cavities.

THE PATHOGENESIS OF ROSACEA: A REVIEW WITH SPECIAL REFERENCE TO EMOTIONAL FACTORS. ROBERT KLABER and ERICH WITTKOWER, Brit. J. Dermat. **51**:501 (Dec.) 1939.

The pathogenesis of rosacea is reviewed with special reference to emotional factors. Fifty cases were studied; 36 patients showed evidence of an abnormal degree of social anxiety, which long antedated the rosacea. This was based on feelings of inferiority, guilt or shame. In 13 cases there was a history of acute psychologic trauma immediately preceding the onset of rosacea, and 20 more patients had suffered from prolonged preceding social or sexual stress, the nature of which was often such as to reactivate the emotional problems of the person. The authors concluded from their study that rosacea frequently results from emotional changes. These may act directly by producing a permanent blushing or, perhaps more often, by lowering the gastric tone which may lead to a permanent flush. Blushing implies an associated and causative emotion of shame or guilt. Flushing, if dependent on emotion at all, is more readily associated with anger. Flushing ordinarily does not suggest the necessity of emotional tone.

ALOPECIA OF THE PERONEAL REGIONS AS A CONSTITUTIONAL SIGN OF A NEURO-ARTHRITIC DIATHESIS. LODOVICO TOMMASI, Brit. J. Dermat. **52**:1 (Jan.) 1940.

In the *British Journal of Dermatology and Syphilis* for November 1938 there is an article by Robertson describing a condition in which an area of atrophic skin occurs on the legs of men. The areas are situated bilaterally and symmetrically below the knees on the anterior, lateral and posterior aspects of the leg. The surface appears smooth, shiny and hairless. Generally men with this disease have also alopecia of the scalp, and the similarity of this alopecia to that of the legs suggests a common causation, probably an endocrine imbalance. Tommasi, who first called attention to the condition in 1928, reviews the subject and describes

the symptoms in detail. They occur often coincidentally, with constitutional signs of neurcarthritism as well as with altered purine metabolism. The condition, he feels, is not dependent on friction and is different from alopecia areata.

RATTNER, Chicago

CLIMATIC OBSERVATIONS CONCERNING LUPUS ERYTHEMATOSUS IN CENTRAL ANATOLIA ALFRED MARCHIONINI, Bull Soc franç de dermat et syph **46** 1030 (Sept-Oct) 1939

In central Anatolia there is intense solar radiation with low humidity (little light filtration) for several months during the year. While actinic cheilitis is common, lupus erythematosus is extremely rare. This fact was advanced as an argument against the belief of some that lupus erythematosus is due solely to solar traumatism.

RESULTS OF PULMONARY ROENTGENOLOGIC STUDIES OF PATIENTS WITH LUPUS ERYTHEMATOSUS L. M. PAUTRIER and SCHAAFF, Bull Soc franç de dermat et syph **46** 1045 (Sept-Oct) 1939

Thirty-seven patients were examined roentgenologically, with the following results. Seven had signs of pulmonary tuberculosis, 2 had signs of old tuberculous pleurisy, and 23 had enlarged hilus nodes, thought to be due to tuberculosis.

Thus a background of tuberculosis was assumed for 86.5 per cent. It was considered indisputable in the cases of 7 of the 37 patients (those presenting signs of pulmonary tuberculosis), as compared with 1 of 21 patients with other cutaneous diseases similarly examined.

TUBERCULIN REACTIONS IN LUPUS ERYTHEMATOSUS L. M. PAUTRIER and A. ULLMO, Bull Soc franç de dermat et syph **46** 1085 (Sept-Oct) 1939

In 42 patients the following reactions were obtained from Mantoux tests with dilutions of tuberculin of 1 to 5,000: 4 very strongly positive, 9 strongly positive, 15 positive, 4 doubtful and 10 (23.8 per cent) negative reactions.

THE TREATMENT OF DARIER'S DISEASE WITH BUCKY RAYS R. J. WEISSENBACH, LEVY-FRANCKEL and J. MEYER, Bull Soc franç de dermat et syph **46** 1339 (Sept-Oct) 1939

The authors mention that Bucky rays have been used frequently in Austria and Germany for the treatment of Darier's disease. Contrary to opinion that the dyskeratoses are resistant to the rays, they felt that these dermatoses are remarkably radiosensitive. The result obtained from a strong erythema dose of Bucky rays administered in five treatments was excellent, all the lesions disappearing and leaving the skin smooth but pigmented.

LAYMON, Minneapolis

EXPERIMENTAL INVESTIGATION ON THE INFLUENCE OF ECZEMATOUS PROCESSES ON PROTEIN METABOLISM K. YOSHIOKA, Jap J Dermat & Urol **43** 141 (June) 1938

Rabbits with experimental dermatitis which were fed casein or amino acids showed diminution in the absolute amount of nitrogen in the blood and in its relative amount in proportion to the ingested nitrogen. The most decided diminution was noted in the acute and early subacute stage of the dermatitis. The amino nitrogen in the blood of the portal vein was also diminished, most considerably on the eighth and on the seventeenth day of the dermatitis. These observations lead to the conclusion that the function of digestion and resorption of proteins is considerably disturbed owing to the dermatitis.

STATISTICAL CLINICAL OBSERVATIONS ON HERPES ZOSTER. K. KATAYAMA, Jap. J. Dermat. & Urol. **43**:145 (June) 1938.

The author analyzes 487 cases of herpes zoster which have been observed in his clinic during the past sixteen years. The greatest number of patients were in the second decade of life. The youngest patient was aged 12 days, and the oldest, 81 years. There was no decided incidence in any one season in preference to the others. The most frequent localization (54 per cent) was the trunk; then followed, in declining order, the face, head and neck (about 29 per cent). The upper and lower extremities were not frequently affected (in about 7 per cent and 10 per cent of cases, respectively). Severe pain was complained of in 233 cases and slight pain in 144; in 47 cases there were no subjective symptoms present. The average duration of the eruption in 222 cases in which the duration was recorded amounted to about seventeen days. One patient died with symptoms of meningitis.

THE EFFECT OF DYES ON YEAST FUNGI. K. HIGUTI, Jap. J. Dermat. & Urol. **45**:125 (June) 1939.

Yeast fungi were most disturbed in their growth by dyes of triphenylmethane structure, like crystal violet and gentian violet. The greatest resistance was shown by mycoderma and, in declining order, by *Saccharomyces*, *Cryptococcus* and *Myceloblastan*. Pathogenic yeasts were relatively less resistant to the dyes than apathogenic ones. Almost all yeast colonies were stained by the dyes contained in the agar mediums. Several species of *Ascomyces*, particularly *Saccharomyces*, formed asci on agar mediums to which certain dyes were added.

LOCAL CONDITIONS FAVORING CUTANEOUS DISEASES. K. KITAMURA, Jap. J. Dermat. & Urol. **45**:139 (June) 1939.

The author reports results of observations and experiments made at his clinic. By means of pharmacodynamic tests it was found that the flexor surfaces of the extremities show a greater hydrophilic, vasomotor and lymphagogue reactivity than the extensor surfaces. The flexor surfaces show greater readiness to manifest pathologic changes than the extensor surfaces. The metameric cutaneous reaction according to Leszczynski-Tomanek was confirmed. It consists in increase in intensity and rapidity of reaction in a certain cutaneous area by preceding irritation of a corresponding area. This was particularly noticed in the wheal produced by histamine. Of interest are also the following clinical observations: an eczematous lesion on a nevus which sharply stopped at the border of the nevus; reddening of corresponding areas on the backs of the hands and of a certain area of the left side of the neck in recurrent attacks of neuralgic pain in the right mandible following extraction of a tooth, which took place four years previously, and limitation of bullous formation to the pigmented areas in a case of *incontinentia pigmenti* Bloch-Sulzberger.

DERMATITIS LINEARIS. S. HUSE, Jap. J. Dermat. & Urol. **45**:145 (June) 1939.

The author has observed in the past ten years 569 cases of linear dermatitis, which is produced by an insect, *Paedrus idae*. The greatest incidence of cases is observed in July. The favorite location is the face (49 per cent) and the neck (22 per cent). The eruption is produced by a poisonous substance contained in the insect and liberated when the person crushes the insect on his skin. Ophthalmologists have reported 86 cases of ocular irritation due to the same insect. The poisonous substance is similar to cantharidin.

BLOOM, New York.

Society Transactions

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

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MAURICE SULLIVAN, M D, *Reporter*

Oct 21, 1939

Light-Sensitive Dermatitis Presented by DR J LAMAR CALLAWAY, Durham, N C

S R, a white man aged 28, a tobacco worker, presents on the face and dorsum of each hand filiform, verruca-like lesions with a translucent appearance, not unlike adenoma sebaceum. When the lesions are exposed to sunlight a severe erythema develops in a few minutes. He is prevented from swimming, playing tennis or engaging in activities that require him to be in the sunshine. A general physical examination gave normal results. Blood counts were normal, and serologic tests for syphilis gave negative results. Studies showed decided sensitivity to light. Coproporphyrin I in the urine measured 0.4960 mg.

DISCUSSION

DR L W KETRON, Baltimore. One could not interpret this condition other than as a peculiar response on the part of this patient to stimulation. Undoubtedly he is light sensitive. The response is somewhat like that in cases of the old so-called dermatitis vegetans. It could not be classified as a nevroid response.

DR FRANCIS A ELLIS, Baltimore. Why could not the condition be both?

DR L W KETRON, Baltimore. Perhaps there is some keloid tissue producing a nodule.

DR L K McCLATCHIE, Washington, D C. Although this case is not a typical one, the diagnosis of helioderma should be considered.

DR RUBEN GOODMAN, Washington, D C. Is there any relation to the light sensitivity in this patient and that seen in patients with pellagra?

DR J LAMAR CALLAWAY, Durham, N C. In spite of large doses of nicotinic acid the patient becomes sunburned as readily as before. The coproporphyrin I content was increased during nicotinic acid therapy.

DR H HANFORD HOPKINS, Baltimore. Last year I had a patient with light sensitivity who was desensitized by gradual exposure to light. The dosage was increased one or two minutes daily until desensitization was complete.

DR J LAMAR CALLAWAY, Durham, N C. This therapy has been tried, and although his tolerance to light increased it was not sufficient to be of practical value.

Erythroplasia of Queyrat Presented by DR J LAMAR CALLAWAY, Durham, N C

This 27 year old white man presents on the glans penis an annular, infiltrated, erythematous patch with a mildly papular border. The lesion has been present for about one year and when first seen appeared to be lichen planus. There was no response to therapy with intramuscular injections of a bismuth compound or with filtered roentgen rays. Dr Fred Weidman examined the histologic section.

and stated that the changes were consistent with those of erythroplasia of Queyrat.

DISCUSSION

DR. PHILIP NIPPERT (by invitation), Atlanta, Ga.: I saw this patient about two months ago. Since that time the lesion on the penis has increased in size, and clinically it is suggestive of erythroplasia.

DR. LEE MCCARTHY, Washington, D. C.: I think one must guard against making a diagnosis of erythroplasia in the case of a man so young. I saw many patients with erythroplasia of Queyrat in France, but all of them were older men. I should consider psoriasis rather than erythroplasia. If the biopsy specimen were taken after roentgen therapy, one would observe these changes. The lesion should not be treated but should be observed.

DR. ADOLPH ROSTENBERG, Washington, D. C.: The most probable diagnosis is a drug eruption. I have seen several patients with lesions similar to this due to drugs. The drug does not necessarily have to be taken internally. It may be by continued contact absorption. I have a patient who had a drug eruption due to a contraceptive preparation used by his wife.

DR. L. W. KETRON, Baltimore: I believe that the condition is psoriasis or seborrheic dermatitis.

DR. FRANK J. EICHENLAUB, Washington, D. C.: Histologically it resembles psoriasis more than anything else.

Exfoliative Dermatitis (Psoriasis). Presented by DR. MICHAEL BOLUS (by invitation), Raleigh, N. C.

W. G., a Negro aged 45, presents a universal exfoliating dermatitis. The eruption began in 1926, at which time he was treated with chrysarobin ointment. He has had yearly exacerbations. This last time the exacerbation was severe and was followed by generalized exfoliation. General physical examination, urinalysis and studies of the blood have given normal results. Following the suggestion of Dr. Raymond Tice, I am giving him weekly injections of 0.5 cc. of alum-precipitated diphtheria toxoid.

DISCUSSION

DR. HARRY M. ROBINSON SR., Baltimore: I have used only phenolized olive oil in similar cases, and the lesions of some patients have responded well. I have never heard of using diphtheria toxoid. I also have given doses of vitamin D, as high as 300,000 units per day. In some patients eruptions respond to treatment with vitamin D, but in many they recur when the administration of vitamin D is discontinued.

DR. L. K. McCLATCHIE, Washington, D. C.: Is there not some danger in giving such tremendous doses of vitamin D?

DR. HARRY ROBINSON SR., Baltimore: Yes, there is, but if one watches the blood calcium value one can guard against bad results. Some patients complain of polyuria and dysuria and have to discontinue taking vitamin D. I believe that if one watched the blood calcium and found no rise above 12 mg. per hundred cubic centimeters one could continue the therapy. Of course, the effects that this type of therapy will have later, such as arteriosclerosis, are not known.

DR. J. W. ANDERSON, Norfolk, Va.: It seems to me that the use of diphtheria toxoid therapy is getting back to the old form of therapy with injections of protein, such as typhoid vaccine and boiled milk.

Leukoderma Aquisitum Centrifugum. Presented by DR. J. LAMAR CALLAWAY, Durham, N. C.

A. Y., a white man aged 27, presents several discrete, oval, deeply pigmented macules scattered over the body and extremities. In the center of each of these is a small brown nevus. The results of general physical examination and studies of the blood were normal.

DISCUSSION

DR I L SANDLER, Washington, D C Do you actually find the nevus cells in the central lesion, and do the nevus cells disappear as the lesion extends peripherally?

DR J LAMAR CALLAWAY, Durham, N C Yes, the nevus cells are localized in the pigmented area The surrounding vitiliginous areas appear normal except for absence of pigment

DR J E GATELY, Baltimore The question of treatment is interesting In removing the nevi, the vitiliginous portion should also be removed Whether or not lesions with hairs in them should be removed is questionable but important

Multiple Benign Cystic Epithelioma Presented by DR J LAMAR CALLAWAY, Durham, N C

CASE 1—Mrs I H, a white woman aged 22, presents discrete translucent papules scattered over the entire face The lesions vary in size from that of a pinhead to that of a pea and have been present since puberty General physical examination and routine studies of the blood show no abnormalities

CASE 2—T R, a Negro aged 25, presents numerous, small, nontender pea-sized to grape-sized nodules on the face and scalp, which are most numerous lateral to the nares and upper lip and less numerous on the outer portions of the face and scalp The results of general physical examination and studies of the blood were normal

DISCUSSION

DR L W KETRON, Baltimore In spite of the fact that these tumors are supposed to be fairly common, a patient has not been seen in many years in whom there were multiple lesions and a history of the disease occurring in several members of the family Single tumors are seen and are sent to the laboratory from our clinic and other clinics, and the patients give a history of multiple benign cystic epithelioma They are not exactly the same lesion from the standpoint of heredity and multiplicity The picture shows, of course, the rudimentary follicles

Sarcoid Presented by DR VINCE MOSELY (by invitation), Durham, N C

B M, a Negress aged 33, presents firm discrete papules and nodules over the entire skin, mostly on the nose, eyelids, neck, forearms, groin and buttocks The lesions about the eyes appear particularly translucent

Urinalyses showed slight albuminuria and hematuria There is mild anemia, and the differential count showed 10 per cent eosinophils The sedimentation rate was 34 mm per hour Chemical examination of the blood showed calcium 10.2 mg, phosphorus 3.6 mg and total protein 8.8 Gm per hundred cubic centimeters, with 2.8 Gm serum albumin and 6 Gm serum globulin per hundred cubic centimeters, and an albumin-globulin ratio of 0.47 The cholesterol amounted to 133 mg and the phosphatase to 7.3 Bodansky units per hundred cubic centimeters Intradermal tuberculin, Frei and brucellergen tests gave negative results Nickerson antigen and various tests for fungi gave negative results Serologic tests for syphilis gave positive results Roentgenograms of the lungs showed widespread small infiltrated areas on both sides Roentgenograms of the bones of the hands and feet showed no abnormalities

DISCUSSION

DR VINCE MOSELY (by invitation), Durham, N C Dr George Harrell, of the department of medicine, Duke Hospital, has done some interesting work on the blood chemistry of patients with sarcoid In all of them he found the serum globulin content elevated He also found the calcium to be somewhat increased in nearly all the cases but no rise in the phosphorus content The phosphatase value was increased With the bilirubin tolerance test he found some evidence of

hepatic damage. There was no relation between the rise in the calcium content or in the phosphatase content and the presence of "cysts" in the bone. In many cases in which there were no demonstrable "cysts" the phosphatase content was increased. Also in several examinations of the urine, protein similar to the Bence Jones variety has been demonstrated.

DR. L. K. McCLATCHIE, Washington, D. C.: I should like to have somebody explain the difference between the ulcerative and the necrotic type.

DR. L. W. KETRON, Baltimore: The clinical picture in this case seems to me to be typical of cystic tuberculosis.

DR. ADOLPH ROSTENBERG, Washington, D. C.: I think the laboratory findings are consistent if Schaumann's views are accepted. He claims that all sarcoids are tuberculous and that there is replacement of bone in all sarcoids, whether or not involvement is detectable by roentgen rays. He says that all the tissues may be affected; for example, if the tonsils are removed, microscopic examination will show the changes of sarcoid.

DR. FRANCIS A. ELLIS, Baltimore: This case illustrates many interesting features. There has been a tendency among certain physicians, especially internists, to get away from the use of the word sarcoid and to regard this disease as a nonulcerative type of tuberculosis peculiar to the American Negro.

DR. H. HANFORD HOPKINS, Baltimore: There is no caseation. The section shows the typical histologic changes of sarcoid. The fact that the roentgenograms were normal does not prove that there was no bony involvement. Twenty-five years ago, in 1914, Schaumann first pointed out that sarcoid was a generalized and not simply a cutaneous disease. The word "cystic" is of course inexact. The term was abandoned in 1920, when histologic studies clearly demonstrated that the bony lesion was never a cyst in any sense of the term but that it was a replacement by solid tuberculoid tissue. Further, many of the American authors, particularly surgeons and orthopedists, have described cystic tuberculosis of the bones as Jüngling's osteitis multiplex cystoides.

DR. RUSSELL FIELD, Washington, D. C.: I have had 1 or 2 patients with extensive sarcoids who responded well to treatment with chaulmoogra oil.

DR. HARRY M. ROBINSON, Baltimore: I should not place too much hope in the chaulmoogra oil. A patient whom I treated with it at the University Hospital was not benefited.

DR. J. LAMAR CALLAWAY, Durham, N. C.: While at the University of Pennsylvania, I had occasion to treat 5 patients with Boeck's sarcoid with chaulmoogra oil and chaulmoogra oil esters (chaulmesterol). None showed improvement.

DR. RUSSELL FIELD, Washington, D. C.: One other remedy I used was acetarsone. Perhaps that accounted for the improvement.

DR. H. HANFORD HOPKINS, Baltimore: Perhaps owing to the fact that sarcoid is a form of tuberculosis, other manifestations of tuberculosis may occur. I think in this case it would be interesting to study the composite picture of the ulcerative lesions to see if they are the typical sarcoid lesions. Possibly the lesions are not benign ulcerative tuberculosis or caseous tuberculosis but tuberculosis in more than one form.

Granuloma Annulare. Presented by Dr. J. M. HITCH, Raleigh, N. C.

Mrs. A. A., a white woman aged 54, was first seen by Dr. E. R. Tyler about two years ago, at which time the diagnosis of granuloma annulare was made. At that time she received five and one-half "erythema doses" of roentgen radiation and a salicylic acid ointment. On the extensor aspects of the left first, second and third fingers are several densely infiltrated annular lesions with depressed centers. The borders of the majority of the lesions form complete rings, while those of others are segments of circles.

DISCUSSION

DR J M HITCH, Raleigh, N C This patient was presented in order to determine whether the members agree with the histologic diagnosis I also considered the diagnosis of erythema annular centrifugum I should like to hear Dr Tyler's opinion

DR E R TYLER (by invitation), Durham, N C I saw this patient several years ago With roentgen ray therapy and mild salicylic acid ointment, the condition cleared up in six to eight months Incidentally, the roentgen ray treatment listed here was not administered to the same lesion but was given to different lesions

DR M H GOODMAN, Baltimore This case is not one of granuloma annulare, because of the age of the patient and other factors, I think it is a case of erythema elevatum diutinum of the so-called Weidman-Besancon type As I recall, there are two types I was helped in reaching this conclusion by the fact that in this case there is a circular lesion on the right hand which is a peculiar dusky purplish red, suggesting a drug eruption The age of this patient and the histologic changes should place this case in the category with those of erythema elevatum diutinum

DR L W KETRON, Baltimore The diagnosis of erythema elevatum diutinum, as a matter of fact, is the correct histologic diagnosis I think, clinically the condition resembles granuloma annulare The section is just a little bit torn and thin If it were thicker and if one had a chance to see the typical deeper structures, one might think of granuloma annulare

DR FRANCIS A ELLIS, Baltimore I think that the condition is granuloma annulare There is some tendency to palisading The section besides being cut too thin has been kept in a strong fixative too long

Keratosis Follicularis Presented by DR JOSEPH A ELLIOTT and DR DAVID G WELTON (by invitation), Charlotte, N C

F C, a white woman aged 29, presents widespread keratosis, most prominent on the hands and feet but involving also the trunk, where the keratosis is follicular and gives a nutmeg grater effect The lesion is distributed also over the arms and legs The palms and soles are beefy red and greatly thickened, and she is unable to close her hands The hyperkeratosis involves the nail beds, so that there are no finger or toe nails Hair is lacking except on the scalp and in the axillae Recently papulopustular lesions have appeared on the back The calcium content of the blood was normal, and serologic tests for syphilis gave negative results General physical examination gave essentially normal results Histologic examination showed findings typical of Darier's disease Treatment has consisted of roentgen therapy, gold sodium thiosulfate, strong keratolytics and many local applications

DISCUSSION

DR DAVID G WELTON, Charlotte, N C This patient is presented for suggestions as to therapy She was treated by Dr Kirby-Smith about six years ago She has had no roentgen therapy except to the lesion on the hand, which by far is the most painful On one occasion I anesthetized her ankle with procaine hydrochloride and attempted to curet away the area of keratosis This treatment was not successful

DR LEE MCCARTHY, Washington, D C I have never observed or heard of a case in which there was so much destruction of the hair The patient says that it has been destroyed since she was 2 years old, but it appears to me as though Darier's disease had not involved the entire scalp

DR H HANFORD HOPKINS, Baltimore This patient shows deformity about her mouth which is highly suggestive of rhagades or syphilitic lesions Another interesting feature is that she has a fresh blister on one ankle Pels and Goodman called attention to this in cases of Darier's disease (Pels, I R, and Goodman, M H Criteria for the Histologic Diagnosis of Keratosis Follicularis

[Darier]: Report of Case with Vesiculation, ARCH. DERMAT. & SYPH. 39:438 [March] 1939).

Dr. HARRY N. ROBINSON Sr., Baltimore: Suggestions as to therapy were asked for. I am not at all in favor of using a gold compound or any of the other more or less potential poisons. One must be careful, because in spite of the fact that the patient has a disfiguring eruption, the roentgen rays can cause somewhat more dangerous lesions. I doubt if anything can be done with much assurance of results.

Dr. I. L. SANDLER, Washington, D. C.: Since some patients with pemphigus have been reported to have been benefited by treatment with tremendous doses of vitamins A and D, I think it might be worth while to give this patient such treatment. Since Dr. Goodman has reported cases of Darier's disease in which the condition is bullous, and since another bullous disease (pemphigus) responds to treatment with germanin, it might be worth while to try this drug, although it is highly toxic.

Dr. FRANK J. EICHENLAUB, Washington, D. C.: I should like to defend the roentgen ray treatment of this disease. A patient whom I treated fifteen years ago with roentgen rays remained well for thirteen years but has now had a relapse. It seems to me that if one can give a patient relief from his disease for that length of time, the treatment is well worth while.

Dr. JAMES R. ALLISON (by invitation), Columbia, S. C.: I should like to make suggestions in regard to the vitamins. I have given large doses of vitamins A and B. I think probably vitamin D is worth while. This patient has had much roentgen therapy. I should like to ask Dr. Eichenlaub if he thinks it is worth while to give her more roentgen therapy.

Dr. FRANK J. EICHENLAUB, Washington, D. C.: I do not know. If she has had as many as four erythema doses, that is enough.

A Case for Diagnosis (Seborrheic Eczema? Familial?). Presented by Dr. J. M. HITCH, Raleigh, N. C.

Mrs. M. S., a white woman aged 26, presents a scaly, greasy dermatitis on the scalp, face, axillas, breasts and groins. This has been present since early childhood, and about 13 members of her family are similarly affected. The results of urinalysis and of routine studies of the blood were negative. Treatment (of this patient and of other members of the family) has consisted of local medication and physical therapy, without permanent improvement. This case is presented because of the familial character and for therapeutic suggestions. (The detailed report on the family will be published later.)

DISCUSSION

Dr. JOSEPH M. HITCH, Raleigh, N. C.: Unfortunately only the 1 patient was seen before the meeting. The case is open for discussion, and I am perfectly willing to change the diagnosis. Dr. Sullivan and others think that the condition is Darier's disease. I should like to hear your views.

Dr. LEE MCCARTHY, Washington, D. C.: I think the condition is Darier's disease.

Dr. FRANCIS A. ELLIS, Baltimore: I think the condition is Darier's disease. The microscopic sections showed nothing particularly diagnostic. I should like to emphasize, however, that sections of Darier's disease in certain stages do not always show the typical changes. The first biopsy specimen from a patient in Baltimore showed no changes. The second section was characteristic. When the lesions begin to dry out, one is not likely to find the specific cleavage which is diagnostic of the disease. A familial history is unusual. I think the diagnosis is Darier's disease, although it could not be made from the sections. I suggest that another specimen be obtained, from one of the new lesions which shows no crusting.

DR MAURICE SULLIVAN, Baltimore Dr Goodman (Goodman, M H Familial Benign Pemphigus, ARCH DERMAT & SYPH 40 273 [Aug] 1939) recently expressed the opinion that the disease described by Hailey and Hailey (Hailey, H, and Hailey, H Familial Benign Chronic Pemphigus, ARCH DERMAT & SYPH 39 679 [April] 1939) under the title benign familial pemphigus was Darier's disease A thorough examination and report of this family would be timely and, no doubt, would lend support to Dr Goodman's contentions

DR M H GOODMAN, Baltimore Darier's disease is prone to have a seborrheic distribution There is another factor occasionally found in cases of Darier's disease, that is, the tendency of the skin to present lesions in the manner of a Kobner phenomenon at sites of injury, similar for example to psoriasis If one bears this in mind, I think it will help in the future to differentiate Darier's disease

DR FRANCIS A ELLIS, Baltimore The patient to whom Dr Ketron referred was first seen by me with what seemed to be a dermatitis on the back of the neck The patient said that the condition recurred every time she wore a sweater and also that it occurred in cold weather A specimen for biopsy was secured from the axillary lesion Dr Ketron said the diagnosis was incorrect More sections from the same block were made, without additional information Moist lesions developed on the back of the neck, and histologic examination of tissue from the neck showed typical changes of keratosis follicularis

A Case for Diagnosis (Verrucous Nevus of the Groin, Hands and Feet)

Presented by DR J M HITCH, Raleigh, N C

O M, a white man aged 25, presents in the groin and over the dorsum of both feet and hands a decidedly thickened, inelastic peculiar "pigskin-type" dermatosis In some areas, particularly over the knuckles and dorsa of the feet, the dermatosis suggests juvenile warts Routine physical examination and laboratory studies gave essentially negative results

DISCUSSION

DR J M HITCH, Raleigh, N C This case is presented for classification I thought the lesion was congenital

DR MAURICE SULLIVAN, Baltimore The lesion has a striking resemblance to epidermodysplasia verruciformis, of Lewandowsky and Lutz Histologically there are dyskeratosis and the peculiar vacuolated cells found in the lesion of epidermodysplasia verruciformis This condition is not a nevus but a dyskeratosis

DR FRANCIS A ELLIS, Baltimore Dr Maurice Sullivan is wrong in saying that this condition is not a nevus Epidermodysplasia verruciformis belongs in the category of nevi There are abnormal changes in the epidermal cells There is some disintegration of the nuclear material The condition may be epidermodysplasia verruciformis, but I should prefer to study the section further before making a final diagnosis

LOS ANGELES DERMATOLOGICAL SOCIETY

CHRIS HALLORAN, M D, *Chairman*

SAUL S ROBINSON, M D, *Secretary*

Nov 7, 1939

A Case for Diagnosis (Lichenoid Eruption Due to Bismuth) Presented by DR IRVING BANCROFT

O D B, a man aged 59, has been receiving intramuscular injections of a bismuth compound intermittently since May 1938 Since May 1939 the bismuth treatments have been given at weekly intervals The history reveals that he

bruised his anterior tibial regions in October 1938. This trauma resulted in the appearance of persistent erythematous areas that were apparently due to circulatory impairment. About three weeks ago numerous small, nonpruritic macules and papules appeared on the legs and buttocks.

Examination shows diffuse erythematous plaques located on the anterior tibial regions. Small red papules and macules, 1 mm. to 3 mm. in diameter, cover the legs and buttocks. Some of the papules are flat topped and resemble lichen planus papules. The Wassermann reaction of the blood was positive in May 1938 and in May 1939.

DISCUSSION

DR. SAMUEL AYRES JR.: Any one seeing the patient clinically, without any reference to the history, would make an unqualified diagnosis of lichen planus. One feature which is a little against this diagnosis is the absence of itching. I think that undoubtedly some lichenoid eruptions are due to bismuth.

DR. IRVING BANCROFT: It seems to me that this man has a thyroid deficiency and low blood pressure, which would indicate the presence of some glandular disturbance. He is receiving thyroid medication at present.

DR. SAUL S. ROBINSON: This patient has lichen-planus-like lesions on the buccal mucosae, which may be in favor of a diagnosis of lichen planus.

DR. CHRIS R. HALLORAN: At the sixty-eighth annual meeting of the California Medical Association in Del Monte, Calif., May 1 to 4, 1939, Dr. Bancroft and I presented a study of 20 cases of pigmented eruptions occurring in patients receiving arsenicals and bismuth preparations in the treatment of syphilis. Clinically and histologically the lesions presented by patients in this study were often indistinguishable from lichen planus. A few patients also presented lesions on the mucous membrane of the mouth that were indistinguishable from those of lichen planus.

Chronic Inflammatory Ulcer of the Leg. Treatment with Sulfanilamide Ointment.

Presented by DR. H. C. L. LINDSAY.

J. N., a white girl aged 16, states that in May 1939 she was bitten by an insect on the right leg. An ulcer developed several days later at the site of the bite. The ulcer appeared on the medial right tibial surface as a dime-sized lesion that rapidly increased in size until it reached 6 inches (15 cm.) in diameter.

Examination reveals an oval bluish purple pigmented lesion with a circular margin on the inner aspect of the right tibial region. The lesion is 6 inches (15 cm.) in length and 4 inches (10 cm.) in width.

Examination of the blood showed 97 per cent hemoglobin and 5,430,000 erythrocytes and 11,450 leukocytes per cubic millimeter. The Wassermann and Kahn reactions of the blood were negative. The urine was normal. Cultures made from the lesion revealed a growth of *Staphylococcus aureus* and *Streptococcus haemolyticus*. The histologic examination showed granulation tissue and fibropurulent exudate. The tissue was widely infiltrated with polymorphonuclear leukocytes. The histologic diagnosis was suppurative inflammation.

The treatment consisted of the local application of an ointment composed of chloral hydrate 5 grains (0.32 Gm.), powdered sulfanilamide 2 drachms (7.8 Gm.), paste of zinc oxide N. F. (Lassar's paste with 10 Gm. of naftalan) 1 ounce (31 Gm.). The ulcer healed in one week after the application of this ointment.

DISCUSSION

DR. SAMUEL AYRES JR.: It is unfortunate that a photograph of the original condition was not taken. This report appears to be a distinct contribution to the treatment of these chronic ulcers. I understand that this lesion has been present

for two months I have also seen chronic streptococcic ulcers healed by administration of sulfanilamide by mouth

DR SUTHERLAND CAMPBELL I doubt that this condition was a true ulcer, for the simple reason that there is no atrophy I do not know of any true ulcers of the skin that can heal without true atrophy There may be a loss of epithelium which simulates an ulcer and which some dermatologists speak of as exulceration It is difficult for me to conceive that this is what one would call a true ulcer of the skin, if one is going to have any true morphologic identity in mind in speaking of an ulcer

DR H C L LINDSAY For the last few years I have been treating scars and improving their appearance so that the average person cannot see where they have existed I presented good illustrations of scar improvement at the last annual meeting of the California Medical Association, in Del Monte (Lindsay, H C L Improvements in Appearances of Scars by Physiotherapy, *Uiol & Cutan Rev* 32 783 [Dec]) 1928) Fungi were searched for microscopically In this case hemolytic streptococcus was found by cultures to be the causative factor producing the ulcer on the leg The ulcer improved about 30 per cent the first night the sulfanilamide ointment was used on it

DR CHRIS R HALLORAN At the Los Angeles County Hospital I have been using sulfanilamide locally in the treatment of chronic ulcers for the past few years The drug may be put up in a 10 per cent paste, using mild paste of resorcinol as a base, or in powder form (10 per cent sulfanilamide in aluminum hydroxide) The rapidity with which healing takes place is often remarkable However, in an occasional case a local sensitivity to the drug will develop after a few weeks of use

Arsenoresistant Syphilis Presented by DR NELSON PAUL ANDERSON

E Q, a white woman aged 34, noted a "pimple" on her face during the early months of 1936 She squeezed the lesion and shortly afterward was given ultraviolet irradiation by a physician Considerable erythema and desquamation occurred on the face and neck after the treatment When the reaction subsided the skin did not assume a normal appearance Numerous flat, round to ovoid, erythematous plaques, with central depressions and elevated, scaling borders, remained At this time the Wassermann reaction of the blood was found to be strongly positive She received two intravenous administrations of an arsenical preparation, and therapy was then discontinued for seven or eight months The Wassermann reaction was still strongly positive at this time Six intravenous injections of neoarsphenamine (0.45 Gm to 0.60 Gm each) were then given, without any change in the lesions except that after each injection the affected areas became larger and more erythematous Her physician then administered thio-bismol once weekly, but the preparation also failed to cause regression of the lesions I first examined the patient on Aug 6, 1937, and a diagnosis of arsenoresistant syphilis was made She received combined arsenic and bismuth therapy, consisting of an arsenical twice weekly and a bismuth compound once weekly One month after starting the combined therapy all the cutaneous lesions were less elevated and were definitely annular Antisyphilitic therapy was continued until April 26, 1938, and the lesions on the forehead, right cheek and forearm disappeared

When the patient was previously presented before the Los Angeles Dermatological Society in May 1938 (*ARCH DERMAT & SYPH* 37 900 [May] 1938), the consensus regarding the diagnosis was that the condition was lupus erythematosus Although the histologic examination at that time was not suggestive of lupus erythematosus and although no improvement resulted from bismuth therapy, the patient was given ten or twelve weekly administrations of gold sodium thiosulfate, also without benefit Malarial therapy was then advised, but because the patient was unable to make arrangements for hospitalization she was given eight to twelve

intravenous injections of typhoid vaccine, resulting in constitutional reactions but without any beneficial change in the cutaneous lesions.

On Sept. 1, 1939, the patient entered the Los Angeles General Hospital to receive malarial therapy. The diagnosis of lupus erythematosus was again made. A second histologic examination failed to suggest lupus erythematosus; the picture was more suggestive of a syphilitic lesion. Staining for spirochetes in tissue gave negative results. The Wassermann reactions of the blood and spinal fluid at this time were strongly positive. The dermatologic lesions consisted of large maculopapular plaques on the temporal areas extending laterally to the external canthi of the eyes, plaques on the right malar region adjacent to the mouth commissure, involvement of the right side of the upper lip and the vermilion border and involvement of the lateral aspect of the neck below and posterior to the ears. An atrophic scar was on the left side of the mouth.

From September 19 to October 11 the patient had ten malarial paroxysms, totaling forty-one and one-half hours of pyrexia with a temperature of 103 F. After the third paroxysm the cutaneous lesions began to disappear. Only a few lesions remained after the sixth paroxysm.

The patient was presented to demonstrate, first, the value of malarial therapy in cases of arsenoresistant syphilis, second, the mechanism of the production of arsenoresistant syphilitic therapy, especially with the arsenicals, and third, the well known fact that arsenoresistant syphilis may give rise to lesions simulating other dermatologic entities, especially psoriasis and lupus erythematosus.

DISCUSSION

DR. IRVING BANCROFT: The scars might be those of lupus erythematosus or syphilis.

DR. H. C. L. LINDSAY: That type of scar can be removed easily by a combination of freezing with solid carbon dioxide and the use of intensive ultraviolet radiation from a water-cooled quartz mercury vapor arc lamp. Care should be taken in selecting cases. Patients with lowered tissue vitality, especially from syphilis, should have their condition improved before this method is used. Healing is apt to be slow and antisyphilitic treatment should continue during the healing stage.

DR. C. RUSSELL ANDERSON: I saw this patient in the wards of the Los Angeles County General Hospital just before she was inoculated with malaria. She had chronic discoid lupus erythematosus and certainly not a syphilid. The response to malarial treatment has been phenomenal. I recall a patient with treatment-resistant chronic discoid lupus erythematosus of the face, whose eruption almost completely disappeared during an attack of varicella. Since that time I have been using intramuscular injections of whole blood and of boiled milk as non-specific measures, often with gratifying results.

DR. NELSON PAUL ANDERSON: I thought this case was interesting because it had been presented before. At that time all the members except myself agreed it was a case of lupus erythematosus, and some still seem to require conversion. With regard to nonspecific measures, I am inclined to believe that any lupus erythematosus that was so extensive would not have melted away as in this case. Furthermore, this patient had a series of at least a dozen intravenous injections of typhoid vaccine, together with a separate series of injections of a gold compound, without the slightest change in the cutaneous condition being effected. There is nothing in the several separate microscopic sections that would support a histologic diagnosis of lupus erythematosus. Finally, the complete disappearance of the eruption after the third malarial paroxysm is additional evidence that the cutaneous condition was a syphilid.

CHRIS R HAILORAN, M D, *Chairman*SAUL S ROBINSON, M D, *Secretary**Dec 12, 1939***Adie's Syndrome Pseudo Argyll Robertson Pupil** Presented by DR BEN A NEWMAN (by invitation) and DR HARRY P JACOBSON

Miss L L, aged 23, during a routine physical examination several months previously, was found to have unequal and irregular pupils, which failed to react to light but reacted in accommodation. The medical and neurologic examinations gave otherwise normal results. Repeated examinations of the blood serum for syphilis gave negative results, and the spinal fluid was normal. She was referred to the dermatologic clinic for an examination and treatment for syphilis.

Examination revealed that the left pupil was dilated and oval. It failed to contract on stimulation by light either directly or consensually but contracted promptly in convergence, with slow dilation thereafter. The right pupil was fixed and failed to react either to light or in accommodation. The condition was considered to be congenital miosis. Reexamination several days later showed the left pupil to vary in size. The patient has no other signs or stigmas of syphilis. The tendon reflexes are variable. The patellar reflex was absent on the right leg and present on the left.

DISCUSSION

DR WALTER SCHWARTZ (by invitation) I am glad to see a patient with this condition. Dermatologists and neurologists have been writing considerably about this disorder. All findings are negative except for the pseudo Argyll Robertson pupil. One would say that the pupils showed typical signs of tabes. I am hesitant, however, to call this condition syphilis, because of the negative Wassermann reaction of the blood and of the spinal fluid. The patient is too young to have a "burned-out" tabes of acquired syphilis. In juvenile tabes, which is uncommon, one certainly would expect to find a positive Wassermann reaction of the blood as well as other signs of congenital syphilis. I agree with the diagnosis of Adie's syndrome.

DR NELSON PAUL ANDERSON I have a patient, a physician, who has the same condition, which apparently was first noticed after an attack of influenza and an infection of the upper part of the respiratory tract. I wonder if there is a possibility that at some time the patient presented might have had diphtheria and that this condition is a residual sequela. It should also be recognized that Argyll Robertson pupils may occur with certain tumors of the midbrain, and I wonder if there is anything in the history to cause consideration of this possibility.

DR H C L LINDSAY The paralysis may have been due to diphtheria. The patient stated that she had had scarlet fever, but the early symptoms of scarlet fever and diphtheria are occasionally confusing. At the Minturne Hospital, East Sixteenth Street, New York, patients are sometimes placed in an observation ward until the final diagnosis is confirmed by the results of laboratory tests.

DR ARTHUR FLETCHER HALL JR As regards the question of an etiologic background, I had a roommate at medical school who presented this condition. He had had tuberculosis of the spine, and the pupil abnormality was never noticed until after a "Hibbs fusion" was performed for treatment of his spine.

DR BEN A NEWMAN (by invitation) The history did not state that the achilles reflexes and the right knee jerk were absent. This is the third case I have observed within the past year, and each patient has presented a similar problem, in that syphilis was diagnosed or suspected. The features of this syndrome are characteristic. The left pupil is more frequently involved, it is

dilated, not miotic; it reacts sluggishly or not at all to light or shade, and the consensual reflex is absent; it contracts rather slowly in accommodation and dilates slowly after the effort to converge is relaxed; it dilates promptly and fully in response to mydriatics, and the condition is most frequently seen in women. There has been no satisfactory explanation for these peculiar pupillary and disturbed tendon reflexes. Adie has expressed the opinion that the condition is a disease *suis generis*.

Dermatophytosis Resembling Contact Dermatitis (Cement and Tar).

Presented by DR. SAMUEL AYRES JR.

J. W. W., a gardener aged 64, has had dry and scaling hands since he was burned fifteen years ago. He has not, however, considered this old burn to have an etiologic relation to his present illness. The patient was first examined on June 3, 1939, for an eruption involving the face, the arms and the ankles of one month's duration. The cutaneous lesions appeared a few days after working on a new job handling cement, although the patient has done this type of work most of his life.

The dermatologic examination, when the patient was first seen, revealed an eruption involving the ankles, especially above the shoe tops, and the flexor and extensor aspects of the wrists. The eruption was eczematized, thickened and scaly. A patch test with the cement handled gave a strongly positive reaction. The dryness and scaliness on the hands were noted at that time, but the patient insisted that he had had this condition for years and did not consider it a part of his present disability.

The treatment consisted of fractional doses of superficial roentgen irradiation and local bland applications. The acute eruption subsided in about two months, and the patient resumed work but did not handle cement. His occupation now consists of working on top of a reservoir tearing off a tar paper roof. About three days after working with tar paper an eruption again appeared and at the time of his visit on October 21 consisted of diffuse erythematous lesions involving the lower part of the face, the back, the sides of the neck and the ankles. The lesions are consistent with a diagnosis of contact dermatitis. A patch test performed with the tar paper gave a strongly positive reaction, and the site was still irritated one week later. For the past five or six weeks the patient has received fractional doses of roentgen rays to the affected areas as well as bland applications. The acute eruption has apparently subsided, although redness and scaling have persisted about the face, neck and hands, without any history of further contact irritation and in spite of adequate local therapy. There is also some dystrophy of the finger nails.

DISCUSSION

DR. IRVING R. BANCROFT: I observed a case of cement sensitization that lasted six years. The patient came to me one day and said that red mercuric oxide would cure him. I procured the red mercuric oxide, and he got well after using it for a short time.

DR. SAMUEL AYRES JR: I am taking unfair advantage of this group for a particular reason. I think that sometimes one can bring out a point by withholding information. This is true when one examines a patient exactly as has been done here tonight. Unquestionably, he has a contact dermatitis. He has an acute eruption and a positive reaction to cement, and I practically cleared up the condition except for that on his hands. I was particularly concerned with the acute condition. After he went to work with the tar paper there was a recurrence on his face and neck, with especial involvement of the ears. He was tested with tar paper, to which he gave a positive reaction. The dermatitis had improved but seems to persist.

Yesterday, I looked at his hands, and something about the nails impressed me as peculiar. I took some scrapings from his hands and nails and found them

to be loaded with mycelium. The man has dermatophytosis of a type I have never seen before. I have seen eruptions due to *Trichophyton purpureum* but never on both hands and never on the face and the ears. Tonight I picked scales off the ears and neck, and they are also loaded with fungi. To me this case is a remarkable diagnostic problem. I have taken cultures, but they became contaminated.

A Case for Diagnosis (Erythema Elevatum Diutinum?) Presented by
DR ANKER K. JENSEN (by invitation)

J. A. M., a man aged 52, complains of an eruption which began two years ago on the anterior surface of the neck as a small, circular, slightly elevated lesion. When the patient was first seen, on July 20, 1939, he presented a firm, slightly raised plaque with a rolled border on the right malar region that extended posteriorly behind the ear and down on the chest. He now presents two active areas, one on the right lateral and posterior surface of the neck the size of a quarter, with slightly raised borders and of doughy consistency, and a similar lesion the size of a dime on the left cheek. The Wassermann reaction of the blood was negative. Treatment consisted of 75 r of roentgen irradiation weekly and the local application of an ointment and a lotion.

DISCUSSION

DR MAX J. WOLFF: Dr. Hall has a case in which the condition belongs in the same category of the erythema group.

DR ARTHUR FLETCHER HALL, JR.: I think that the lesion on the right side of the chest, if that is part of the clinical picture, looks entirely different from the other lesions. It is different from the lesion on the back of the neck, which I assume is representative of what is being presented. The lesion on the chest suggests ringworm. If I am correct in my idea of what the term means under which this case was presented, I have understood the condition to be one of the granuloma annulare family rather than one of the erythemas. I had also considered that the condition in the case that I presented under the title erythema elevatum perstans was not of that family but remotely related to erythema multiforme. I think that a histologic examination would be interesting, because the granuloma annulare family would probably be identified by a microscopic examination.

DR H. C. L. LINDSAY: If this patient has erythema multiforme, mercuric cyanide ($\frac{1}{16}$ grain [0.01 Gm.] ampule) might be injected on alternate days for a few doses. Mercuric cyanide acts as a specific remedy in some cases (*Pennsylvania M. J.* 33:533, 1927).

Darier's Disease Presented by DR SAMUEL AYRFS, JR. and DR NELSON PAUL ANDERSON

B. S., a white girl aged 7 years, has had an intermittent eruption on the neck for the past four years. On three occasions this eruption has spontaneously disappeared, and the site apparently remained clear for about one month. The mother is unable to recall the conditions under which it disappeared the first two times. The last disappearance was in February 1939, when the child had an appendectomy.

The examination shows a blotchy, dark brown, warty eruption on the anterior lateral and posterior aspects of the neck, composed of small papular lesions. A small comedo-like body was present in the summit of many papules. On the palmar surfaces, especially on the right thenar eminence, were a few scattered, pinhead-sized, yellow-brown, intraepidermal papules. Two similar keratotic lesions were on the plantar surfaces. The microscopic picture is typical of Darier's disease.

DISCUSSION

DR NELSON PAUL ANDERSON: The child was seen about six weeks ago, at which time a histologic examination was made and she was given 75 r of roentgen

radiation. The mother tonight tells me that two or three weeks after the patient returned home the eruption cleared, and the skin stayed clear until about two weeks ago. It seems unusual for Darier's disease to present such exacerbations and remissions.

A Case for Diagnosis (Lipoidosis? Necrobiosis Lipoidica Diabeticorum?). Presented by DR. MAX J. WOLFF.

D. P., a Jewish housewife aged 65, has had diabetes mellitus for the past six or seven years. Until two years ago she had taken insulin, 5 international units twice daily for two years. The diabetic condition is now controlled by diet alone. The patient presented herself for the treatment of an eczematoid dermatitis on the right forearm, and during the course of a routine examination a waxy yellow, infiltrated plaque, 4 by 2 inches (10 by 5 cm.) in size, was discovered on the left lumbar region.

The examination of the blood showed: 103 per cent hemoglobin, 5,240,000 erythrocytes and 11,950 leukocytes per cubic millimeter, with a color index of 0.99. A differential count showed 55 per cent polymorphonuclear neutrophils, 50 per cent lymphocytes, 4 per cent monocytes and 1 per cent eosinophils. Chemical examination of the blood showed 128 mg. sugar and 270 mg. cholesterol per hundred cubic centimeters. The Wassermann reaction of the blood was negative. The urine was normal. The basal metabolic rate was + 1 per cent.

DISCUSSION

DR. NELSON PAUL ANDERSON: An interesting feature of this case is the presence of definite changes in the skin of the lower middle part of the lumbar region. In this area was a typical shagreen patch, which ordinarily is associated with adenoma sebaceum and tuberous sclerosis. It is one of the stigmas of degeneration and, as far as I know, has not been described with any disease except Recklinghausen's disease, adenoma sebaceum and tuberous sclerosis. As far as the patient can remember, she has had this patch on the left side of her back for her entire life. What connection this lesion has with the diabetes is problematic. From the histologic section, I do not believe that the condition is necrobiosis lipoidica diabeticorum, but undoubtedly this disease can present many different pictures. Nevertheless, the histologic section is peculiar, in that there is decided infiltration of fat cells and fatty material extending into the cutis. I think this condition may be a new disease entity or a known disease masquerading under another name.

CHRIS R. HALLORAN, M.D., *Chairman*

SAUL S. ROBINSON, M.D., *Secretary*

Jan. 9, 1940

Erythema Multiforme Limited to the Plantar and Palmar Surfaces. Presented by DR. IRVING R. BANCROFT.

H. B., aged 49, complains of an eruption on the palmar and plantar surfaces present since Dec. 30, 1939. He had an infection of the upper part of the respiratory tract and pharyngitis for ten days preceding the eruption. The examination on Jan. 2, 1940 revealed bright erythematous, tender, macular lesions on the plantar surfaces. The feet were greatly swollen, and the patient could not wear shoes or walk. On January 3 the palmar surfaces also became red, swollen and painful. The lesions began to fade on January 6, but the feet are still swollen and painful and show some residual plantar erythema.

DISCUSSION

DR SAMUEL AYRES JR I think the condition in this case is a toxic eruption probably belonging in the erythema multiforme group following an acute infection of the throat

DR IRVING R BANCROFT The peculiar thing about this condition is that the eruption on the feet almost cleared but now lesions have suddenly appeared on the hands, ten days after the onset

Dermatitis Medicamentosa (Phenobarbital? Carbarsone?) Presented by
DR H C L LINDSAY

C B W, a white woman aged 73, complains of an eruption of three months' duration. The condition began with circinate, papular lesions around the waist and then spread to the legs, the shoulders, the arms and the face. One round lesion appeared on the hard palate. She had been treated for "nervousness" by several physicians and was receiving phenobarbital. She also received carbarsone (paracarbamunophenylarsenic acid) for intestinal parasites. The cutaneous lesions appeared first to be those of erythema multiforme, but they now appear to be a dermatitis exfoliativa. She has been hospitalized for the past six weeks and received sodium thiosulfate intravenously and autohemotherapy. The lesions have almost entirely disappeared, and she now presents the picture of a mild generalized exfoliative dermatitis. The examination of the urine for arsenic gave negative results.

Psoriasis Limited to Palmar and Plantar Surfaces Presented by DR
ARTHUR FLETCHER HALL JR

W F, a student aged 20, was first examined on Sept 12, 1939, for a diffuse thickening and scaling of the palms and soles of two years' duration. The lesions appeared at the onset on the finger tips and then gradually involved the palmar surface of the hand and the fingers. Similar lesions appeared on the plantar surfaces, especially on the pressure areas. A fine, snow white, powdery scaling is evident when the palms and soles are dry, especially in the natural folds of the hands and fingers. The patient was working with model airplane "dope" at the time of onset, but there has been no contact with this material for over one year. The condition became worse during and after a two week automobile trip but improved during the summer when he was sailing his boat.

Examination of the urine gave normal results, including a Gutzzeit test for arsenic. Culture on Sabouraud's medium showed no growth. The histologic examination showed considerable hyperkeratosis, areas of parakeratosis and decided acanthosis with palisade arrangement of the papillae. Some round cell infiltration was present in the pars papillaris and the upper part of the corium.

The patient states that he received twelve to fifteen weekly treatments with roentgen rays during the first year of the disease, with little benefit. Internally, he has been taking vitamin B complex in the form of "Galen B" for about nine months. There is no history of the ingestion of arsenic. He is now on a low fat diet and uses an ointment containing juniper tar, salicylic acid and precipitated sulfur, equal parts, up to 1 ounce (28.4 cc). Internally, he receives percomorph liver oil, 20 drops twice daily, and the vitamin preparation.

DISCUSSION

DR SAMUEL AYRES JR This case is interesting because there are so many examples of hyperkeratotic dermatitis involving the palms and soles which do not fit in with fungous disease, contact dermatitis or ordinary allergic manifestations. There is some toxic disturbance of undetermined nature, possibly a vitamin deficiency.

DR WALTER SCHWARTZ (by invitation) I have not seen any one being extremely dogmatic in diagnoses in these cases. The diagnosis of psoriasis is

infrequently suggested. To support the possibility of psoriasis in this patient is the history of a scaling lesion on a knee some time ago. I think psoriasis is to be seriously considered.

DR. H. SUTHERLAND CAMPBELL: On looking at the lesions, I believed them to be a possible fungous infection or psoriasis. The patient mentioned that he had spots on the hand that cleared up. I think that the results of histologic examination are conclusive in this case. I do not believe one could see such classic elongated papillae in any section other than one of psoriasis.

DR. KENDAL FROST: I treated this boy for several weeks last year and gave him the roentgen irradiation referred to. His hands were irritated most of the time from handling ropes on his sail boat, and it was difficult to differentiate the various factors making up the appearance at that time. He now has a definite psoriasis on the plantar surfaces, and he must have had it all the time.

DR. ARTHUR FLETCHER HALL JR.: Psoriasis was considered in the original diagnosis because of the silvery scales present on the palmar markings and on some areas of the feet when the skin was dry. The histologic picture seemed characteristic enough of psoriasis to make that diagnosis. In so far as the sailing is concerned, as long as he has been under my care I have found that his hands are better when he is out in the sunlight. When he made a two week automobile trip, during which he was under considerable nervous strain, the hands were worse. Last fall he attended college and was apparently under considerable mental pressure and strain from his studies. His hands got worse during that time. At Christmas time his family decided that he had better stop his studies and do some work that did not upset him, in the hope that his hands would benefit in some way. Since he has been working as a contractor the hands have become much worse, and I am at a loss as to how to treat him. He can hardly use a pencil with his hands.

Pachyonychia Congenita in Mother and Daughter. Presented by DR. NELSON PAUL ANDERSON.

L. L. K. and M. L. K., mother and daughter, aged 28 years and 3 years and 9 months, respectively, are presented for a disorder affecting all of the nails. The mothers' nails have been involved since early childhood, and no benefit has been derived from surgical removal of the nails, radium and roentgen irradiation or numerous keratolytic ointments. No other relatives have a similar condition. The child has had the disorder since a few weeks after birth.

The examination reveals all of the nails of both patients to be greatly thickened and extremely hard. The nails are apparently of normal length and width and become thicker at the free borders, where they measure 3 to 5 mm. in thickness. On the mother's plantar surfaces are many callosities. Examination of the scalps of both mother and child gave normal results.

DISCUSSION

DR. NELSON PAUL ANDERSON: This is the first example of pachyonychia congenita that I have seen. It is certainly congenital, as one can observe the same changes in the nails of the daughter, although she has no changes in the mucus membrane or callosities on the soles.

Keratosis Palmaris et Plantaris. Presented by DR. FRANKLIN I. BALL.

H. B., a nurse aged 38, is presented with her sister, M. B., aged 44, for a papular eruption on the palms and soles present since early childhood. The lesions have become more pronounced during the past two years. A third sister is also said to have similar lesions.

The dermatologic examination shows numerous, scattered, split pea-sized, flat, hyperkeratotic papules on the palmar and plantar surfaces.

The examination of the urine showed a positive result of a Gutzeit test for arsenic in both sisters. The laboratory report states "amount greater than 1 mg per liter." A histologic examination of a section from the palm of H. B. showed all the cutaneous layers to be uniformly thickened, with excessive but normal cornification.

DISCUSSION

DR SAMUEL AYRES JR. I think the disorder is consistent with the diagnosis of arsenical keratosis, even though there is no history of ingestion of arsenic. There is no record whether the lesions were present at birth or not.

DR ARTHUR FLETCHER HALL JR. I was intrigued by the fact that the lesions looked like arsenical keratoses. Examination of the urine for arsenic gave definitely positive results for both sisters. It seems much more than a coincidence that 2 sisters should have lesions which are clinically arsenical keratoses and also have positive reactions for arsenic in their urine.

DR NELSON PAUL ANDERSON. I believe that these small punctate keratoses are not due to arsenic. Michael, about six or seven years ago, had an interesting paper on this particular group of keratoses (Michael, J. C. *Keratoderma Dis-seminatum Palmaris et Plantaris*, *ARCH. DERMAT. & SYPH.* 27:78 [Jan.] 1933). The fact that these lesions came on so early in life would seem to speak for a congenital origin.

DR H. C. L. LINDSAY. This subject has been discussed before. I had occasion to investigate the death of a patient whom I suspected to be poisoned by arsenic. Arsenic was found in the urine. The coroner informed me that many people had arsenic in their urine in this district. Two of his men had arsenic demonstrable in their hair, although they could not trace its source. Neither of the men was taking arsenic. It may be that arsenical solutions are still being used to spray vegetables to destroy parasites.

DR FRANKLIN I. BALL. It is my opinion that although arsenic has been found in the urine of both sisters, these lesions are probably not due to the arsenic but represent the congenital form of papular keratosis.

Carotinemia Presented by DR SAMUEL AYRES JR.

E. L., a woman aged 25, has had yellow palms and soles for six or seven years. The disease has been continuously present but is apparently more pronounced during the summer. The patient states that she ate carrots four or five times a week up to four years ago and has had none since. She eats ten or twelve oranges a day, squash about four times a week and lemons practically every day. When the patient was first examined, in July 1938, there was a yellowish orange discoloration of the palms and soles. The phalangeal joints were involved to a lesser extent. The calloused areas were more deeply pigmented. Examination of the scleras gave negative results. The patient was told to avoid all foods containing yellow pigment. She has been observed on numerous occasions since her first examination, and the discoloration appears to be fading. When examined tonight, however, the palms, the soles and the backs of the fingers still appear to be definitely yellow and somewhat more pink than normal.

The test for blood carotene (Johnson) gave a positive result on July 22, 1938, on Sept. 7, 1939 and on Jan. 9, 1940.

DISCUSSION

DR BEN A. NEWMAN (by invitation). There are two questions concerning this abnormal pigmentation about which I have been unable to find any satisfactory answers. First, why is this normal lipochrome pigment of the blood stream excreted through the sweat glands rather than through the sebaceous glands, and second, what are the local factors responsible for depositing this pigment in the epidermis? That there must be some local factor responsible for this deposition is obvious, since patients with much higher percentages of this pigment in the blood stream but without carotenemia are not uncommonly seen.

DR. H. C. L. LINDSAY: Why is carotenoid pigmentation so selective that it does not affect the eyes as many other pigments do?

DR. CLEMENT COUNTER (by invitation), Long Beach, Calif.: I think it is rather interesting that this woman continues to have calluses on the palms, in spite of the fact that she does not do housework or other manual labor.

DR. SAMUEL AYRES JR.: The color is more discernible if one puts one's own hand beside hers. I think the pigmentation is not as pronounced as it was one year ago. The treatment of carotenemia, according to authorities, is to exclude foods that contain carotene. It is over a year since she has excluded those foods, and there is still a great deal of pigment present. I should like to know if any one has any further suggestions as to treatment. I am glad to have the suggestion of using thyroid medication.

CLEVELAND DERMATOLOGICAL SOCIETY

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JAMES R. DRIVER, M.D., *Reporter*

Jan. 25, 1940

Xanthoma Tuberosum. Presented by DR. H. G. MISKJIAN.

J. D., a well built, tall man in his forties, about ten years ago had several attacks of epigastric pain with vomiting, which were supposed to be due to indigestion. He had no further trouble until about six months ago, when he experienced some gastric distress with gas and acute pain. Roentgen examination within the past two weeks revealed cholelithiasis. For fifteen or twenty years he has had tumors on his elbows and knees. He also had several tumors on his buttocks, but these lesions have disappeared. In 1915 he suffered from septicemia, the result of an "abscessed ear," which kept him in the hospital for seventy-three days. In 1934 the second and third fingers of his left hand were badly cut by a rip saw. Stitches were put in. About a year later small tumors, thought to be keloids, began to develop on these two fingers.

The second and third fingers of the left hand show numerous small, red tumors. Most of them are on the volar surface of the fingers, but there are also some on the dorsal surface. A few have developed in a row along the linear scars on the fingers. The tumors are about the size of a bean or a pea. By their fusion they form bright red, irregular, raised, hard masses, resembling keloids. Close examination, however, reveals in them small deposits of a yellowish white substance, about the size of a pinhead and often larger.

About in the center of each palm there is a round, dime-sized, slightly raised, yellowish pink plaque of xanthoma. These lesions manifest perfect symmetry. On the knees and elbows there are characteristic tumors of xanthoma fused together in protruding masses, varying in size from that of a bean to that of a walnut. Some of them are slightly pedunculated.

On the left buttock there are five or six slightly raised, yellowish nodules, approximately 1 cm. in diameter. The blood cholesterol was 438 mg. per hundred cubic centimeters. The urine gave a negative reaction for sugar. The patient refused permission for a biopsy.

DISCUSSION

DR. H. G. MISKJIAN: I have presented this case, first, because it illustrates the association of xanthoma tumors with disease of the gallbladder. Hypercholesteremia was probably the primary factor, giving rise to the deposits in

the skin and perhaps later to the gallstones. The second reason for presenting the case is the role traumatism appears to have played in determining the localization of deposits of cholesterol in the scars of the injured fingers.

Dermatitis Exfoliativa Presented by DR BENJAMIN LEVINE and DR I L SCHONBERG

B T, an intelligent man aged 38, stated that at the age of 8 years he had either ringworm or favus of the scalp, for which he received roentgen therapy in Antwerpen, Belgium. This condition was followed by alopecia, with atrophy and roentgen dermatitis. When he was 17 severe sycosis vulgaris of the beard developed, which was treated with numerous exposures to roentgen rays, resulting in roentgen dermatitis, with atrophy, telangiectasia and keratoses. One area on the left malar region was treated some years later for epithelioma. Ten years ago dermatitis exfoliativa developed, which has persisted. He has been in hospitals all over the country, from California to New York. Prior to coming to us he had been in Mount Sinai Hospital in New York, where he received fever treatments in a cabinet. He showed decided improvement after that type of therapy, but within a few weeks the eruption recurred. Subsequent fever therapy with typhoid vaccine resulted in a remission lasting almost two years. In the past two years this type of treatment has not benefited him. He has improved at times by fasting, only to have the eruption exacerbate when he started to eat again.

There is a generalized, pruritic, scaly, erythematous, lichenified dermatitis. The face is moderately edematous. On the face and scalp there is evidence of chronic roentgen ray dermatitis. The regional lymph nodes are moderately enlarged. The spleen and liver could not be palpated.

There were 4,300,000 erythrocytes and 12,000 leukocytes per cubic millimeter and 80 per cent hemoglobin. The differential blood count showed 64 per cent polymorphonuclear leukocytes, 14 per cent small lymphocytes, 6 per cent large lymphocytes and 16 per cent eosinophils.

Several specimens have been taken from the areas of exfoliative dermatitis for histologic examination, and all showed the epithelium to be moderately to considerably thickened, with many blunt, deep rete pegs. Thickening was due chiefly to proliferation of the prickle cell layers. There was no appreciable keratinization of the superficial cells. In places superficial epithelial cells showed considerable vacuolation of the cytoplasm. The papillae were of average size and showed slight to moderate round cell infiltration. At one end of the section there was a small amount of keratinized squamous cells, partly separated from the nonkeratinized portion suggestively by edema. The underlying corium showed slight to moderate edema and moderate perivascular cellular infiltration. These cells consisted chiefly of lymphocytes and endotheliocytes, but a small number of eosinophils were prominent.

DISCUSSION

DR CLYDE L CUMMER: This patient showed adenopathy in both axillae. The differential blood count is abnormal, as shown by the ratio of small lymphocytes to large lymphocytes. Further study from the standpoint of one of the lymphoblastomas is indicated.

DR BENJAMIN LEVINE: We have kept in mind the possibility of lymphoblastoma. This same ratio of lymphocytes has been present in several examinations.

Lichen Planus with Pigmentation of the Face Presented by DR FRANK McDONALD

A L, a youth aged 18, about six months ago noticed an eruption on the dorsa of his hands. Shortly thereafter the face and neck became involved. He had worked for five and one-half months in a CCC camp. The condition was

attributed to excessive carbohydrate ingestion by the camp physician and was treated with a white ointment without benefit. Three months ago the hands began to clear up spontaneously, but the face and neck have remained unchanged. There has been only occasional pruritus. No previous attacks had been experienced, and no cutaneous disease was known among the patient's associates. No drugs had been taken; there were no constitutional symptoms, and no history of an emotional upset was elicited.

In general the patient was well nourished, well developed, moderately intelligent and placid. Examination of the teeth showed partial artificial dentures, with caries in many of the remaining teeth.

The lateral and to a slight degree the posterior aspects of the neck present numerous, discrete, pinhead-sized, pink, flat-topped, polygonal-sided papules, some of which are shiny but most of which have a dull luster. The papules on the neck tend to be contiguous but not confluent. The butterfly area of the face, especially the forehead, perilabial area and chin, show a diffuse, reddish brown pigmentation, with sharply defined, arciform borders. There is a suggestion of atrophy. Follicular plugging is absent. Occasionally at the borders of this pigmentation there are a few papules that look like those on the neck. At the corners of the mouth there are small, white, membranous patches. The dorsa of the hands and wrists show a mild, violaceous mottling. The dorsa of

A hemogram, the results of urinalysis and roentgenograms of the chest were normal.

Tissue was removed from the neck and from the forehead, and the histologic appearance was similar. The epithelium was somewhat atrophic uniformly. The rete pegs were not prominent. A rather patchy infiltrate of lymphocytes, plasma cells and large mononuclear cells with edema was seen in the papillary and subpapillary areas, some of the areas suggesting a bandlike formation. No giant cells were found. Perivascular inflammation was not present. In some areas there were small phagocytes containing golden brown pigment, which on differential staining was shown to be melanin, not iron. The deeper subcutaneous tissue was normal.

DISCUSSION

DR. JOHN A. GAMMEL: I thought the lesion on the face was seborrheic dermatitis.

DR. H. J. PARKHURST, Toledo: The present appearance and the localization of the lesions, including those on the wrists, are more suggestive of fading lupus erythematosus than of lichen planus. However, I found a flat papule on the side of the neck, and that, with the histologic picture, of course, is in favor of lichen planus.

DR. FRANK McDONALD: I have presented this patient chiefly because of the associated pigmentation. Clinically and histologically the papular eruption was lichen planus. The pigmentation is unusual. Crocker (*Brit. J. Dermat.* 12:421, 1900) has described a type of the disease, which he called erythematous lichen planus, in which reddish or pink pigmentation is present.

Chronic Chancroid of the Vulva, Perineum and Inguinal Regions. Presented by DR. JAMES E. ENGELER (by invitation) and DR. GERARD DE OREGO. A. Z., a Polish woman aged 61, has complained of pain and draining sinuses of the perineum and both inguinal regions for about one year. She has had a swollen abdomen and shortness of breath for a similar period. There was a history of chronic alcoholism.

General examination showed her to be well developed but poorly nourished and somewhat emaciated. The fundi showed sclerosis of the vessels, with remote hemorrhages. The area of cardiac dulness was moderately enlarged. The blood pressure was 140 systolic and 80 diastolic. There were no cardiac murmurs.

There is a destructive, painful and bleeding ulcerative process involving the vaginal wall, labia and perianal regions. The surface of the ulceration is covered with a foul, grayish white exudate. Multiple inguinal sinuses are present bilaterally.

The patient has secondary anemia, but otherwise the hemogram was normal.

Repeated smears from the ulcer and sinuses have been negative for tubercle bacilli, gonococci, Ducrey bacilli and Donovan bodies. The Frei test gave a negative result. The reaction to the tuberculin test (human tuberculin in a dilution of 1:1000) was 1 plus. The "formal gel" test gave a negative result. The Ito-Reenstierna reaction was 1 to 2 plus. The serum albumin was 2.2 Gm per hundred cubic centimeters and the serum globulin 4.4 Gm (albumin-globulin ratio 0.5). The Kline test of the blood and of the spinal fluid gave negative results. Roentgenograms of the chest and pelvis were normal.

Histologic examination of tissue removed from the edge of the ulcer revealed an acute and chronic granulomatous inflammation, with ulceration of the epi-



Case of chronic chancroid of the vulva, perineum and inguinal regions

thelium. The process was consistent with the changes seen in cases of chancroid. No changes suggestive of malignancy were noted.

DISCUSSION

DR CLYDE L. CUMMER: I should like to ask whether anaerobic cultures have been made of these ulcers. The character of the ulceration suggests somewhat that produced by the anaerobic streptococcus.

DR GERARD DE OREO: We have made ordinary cultures. There was no growth in anaerobic mediums.

DR HAL ELSON FREEMAN: By a process of elimination I conclude that this case is one of chronic chancroidal infection.

Cheilitis Exfoliativa Presented by DR BENJAMIN LEVINE and Dr I. L. SCHONBERG

M. M., a woman aged 19, has had chronic cheilitis exfoliativa for three or four years. There has been no response to many different forms of medication,

including roentgen therapy. At times the eruption would spread into the mouth and on the tongue. She had gingivitis at times, which prevented her from eating. She had been hospitalized and put on a high vitamin diet, but at times she was unable to retain any food because of nausea and vomiting. She presented some vague abdominal symptoms, and the internists at the hospital were unable to differentiate between appendicitis and irritation of the whole gastrointestinal tract. When she was on a high vitamin diet with the addition of thiamine chloride and riboflavin some improvement was noted. Since that period in the hospital she has had a uterine suspension and her appendix removed. After this the disease of the lips and mouth cleared up. However, she is still taking vitamin B complex.

DISCUSSION

DR. H. N. COLE: Does the patient smoke?

DR. BENJAMIN LEVINE: No.

DR. I. L. SCHONBERG: At one time during the course of her treatment we considered the possibility of sensitivity to mercury. Traub and Holmes (ARCH. DERMAT. & SYPH. 38:349 [Sept.] 1938) wrote a paper on the effects of amalgam fillings causing cheilitis. Patch tests were made with mercury, with negative results. The amalgam fillings are still in her mouth.

DR. EARL W. NETHERTON: This patient continued to take vitamin B therapy after she left the hospital. How do you attribute the improvement to the operation to which there is no conceivable connection? I believe the patient is suffering from a vitamin B deficiency.

Dermatitis Herpetiformis. Presented by DR. BENJAMIN LEVINE and DR. I. L. SCHONBERG.

J. D., a white woman aged 22, for the past three years has been suffering from a pruritic eruption, which appears in successive crops on various parts of the body.

There are groups of papulovesicular lesions. Most of them are about the waist. Over the rest of the body there are whitish scars due to excoriations. Lesions also are present on the head, arms and legs. The patient also has coarctation of the aorta.

Histologic examination showed in the epidermis and immediately below it small vesicles filled with fibrin and polymorphonuclear leukocytes. The squamous epithelium regional to the vesicles showed degenerative changes, cells in some places necrotic and in other areas showing large vacuoles, with the nuclei poorly stained and the cell outlines blurred. There was some diffuse infiltration of the papillary projections by polymorphonuclear cells. Some edema of the cutis was present. At a distance from the acute vesicular lesions there were mantles of cells about blood vessels in the cutis, with eosinophils and small round cells about equal in number. There was a thin layer of cornified cells covering the epidermis. Two additional sections taken from various levels of the block showed similar pictures.

DISCUSSION

DR. J. EDGAR FISHER: I had the opportunity of seeing this patient last summer, at which time there was severe involvement with dermatitis herpetiformis. It was necessary to hospitalize her at that time, and a partial remission followed.

An Unusual Case of Keratosis Suprafollicularis with Pili Incarnati Inciting Foreign Body Reaction. Presented by DR. H. H. JOHNSON.

P. M., a student nurse aged 26, has noted a papular eruption on the extensor surfaces of her arms and forearms and the extensor surfaces of the legs and knees for five years. The patient, who is a careful observer, stated that the lesions have been neither painful nor pruritic and that the individual lesions

began as pale, rather deep papules, which subsequently became moderately erythematous and covered with a flat scale, which scrubs off with bathing. The lesions subsequently regress, leaving a brownish pigmentation, which persists for several months, and ultimately a slight scar.

There was a history of roentgenographically proved duodenal ulcer in 1937, and there have been frequent infections of the upper part of the respiratory tract for several years. Otherwise the patient has been in good health.

The physical examination showed no abnormalities with the exception of the cutaneous lesions.

There are many deep-seated papules 2 to 3 mm in diameter, varying from normal color to dull pale red or light brown, in the skin of the extensor surfaces of the arms, forearms, knees and legs. There are many other lesions showing smooth, thickened, adherent, brownish hyperkeratosis, the removal of which reveals widened follicular openings, from many of which can be removed fine colorless hairs. There are many light brown areas of pigmentation at the site of former lesions, and some of these areas show slight atrophy. Among these lesions there are many normal hairs.

The hemogram and the results of urinalysis were normal. Serologic tests for syphilis gave negative results in May 1937. The Mantoux test was negative with a dilution of 1:10,000 and positive with a dilution of 1:1,000. Roentgenograms of the chest showed the pulmonary fields to be clear.

Histologic examination of a papular lesion on the leg showed hyperkeratosis and a follicular keratotic plug descending for some distance into a widened follicular opening. In the papillary portion of the corium the follicle was angulated at 45 degrees. In the reticular corium there was a small discretely localized but not encapsulated granuloma, containing mature connective tissue cells and rather densely infiltrated with lymphocytes and mononuclear cells. Foreign body giant cells were present, arranged in small foci within the granuloma. Near the horizontal borders of the granuloma there were five pale yellow oval bodies showing the same staining reaction as the hair (and corresponding in size to the fine hairs extracted from one of the papules). These were apparently cross sections of a coiled hair within the granuloma.

DISCUSSION

DR H. N. COLE: I had previously made a diagnosis of papulonecrotic tuberculid in this case, but today I am not so sure. There are present on the extensor surfaces of the arms and legs many scaly papules which are not pruritic and which clinically suggest parapsoriasis. However, the histologic picture does not bear out this diagnosis.

DR E. W. NETHERTON: The follicular character of the eruption suggests the possibility of vitamin deficiency. Has the presenter made any investigations along this line?

DR H. H. JOHNSON: I plan to investigate this possibility.

DR H. J. PARKHURST, Toledo: I am inclined to favor a diagnosis of keratosis suprafollicularis.

Psoriasiform Parakeratosis (Brocq), Dry Type Presented by DR H. G. MISKIAN

A S., a well nourished unmarried woman aged 23, has had a generalized eruption for three and a half years. It first appeared in the form of a patch on the right elbow. This disappeared after the application of an ointment. Another patch developed later on the anterior surface of the right leg and became thick and scaly. During the past five months the eruption has spread. It has been intensely pruritic. Local applications on the advice of physicians have had no appreciable effect. She has been taking no drugs internally.

The eruption is of the erythematous squamous type. It predominates on the lower extremities, while the trunk is practically free. Around the elbow joints, extending upward on the arm and below on the forearm there are large, confluent, dry, red patches, covered with fine, branlike scales. The borders are sharply defined but not raised. There is no trace of infiltration on palpation. The patches occupy almost the whole circumference of the elbows, leaving only a narrow band of normal skin on the flexor surface. Scattered around the main patches on both sides are a number of smaller, more or less rounded lesions of the same type.

On and around both trochanteric regions there are extensive confluent patches, covering an area about 20 to 25 cm. in diameter. These are of the same type as the eruption on the legs except that their borders are less sharply defined and on their surfaces there are numerous shallow cracks in the epidermis, which seem to be due to the dryness of the skin and to the greater thickness of the scales in this region.

The anterior surface of the right leg is occupied in its middle three fifths by a roughly oval patch, measuring 15 by 9 cm., with fairly sharply defined borders. It is dark, brownish red, with thickening of the skin, covered with rather heavy scales separated by superficial fissures. It looks like a chronic lichenified dermatitis.

Scattered over the thighs and the posterior surface of the legs are numerous round, sharply defined, erythematous squamous elements about the size of a quarter. Their features are the same as those of the aforementioned larger patches. They are all discrete. There are, however, a few that are more extensive and more irregular in shape and that form a transition between the nummular elements and the confluent areas.

The eruption in general resembles psoriasis somewhat, but close study of the lesions, particularly by systematic scraping of the elements, enables one to rule out such a diagnosis.

DISCUSSION

DR. E. W. NETHERTON: The eruption suggests parapsoriasis, but one should also consider the possibility that the condition might eventually turn out to be mycosis fungoides. The lesions are not unlike the prefungoid stage of that disease. The intense itching does not fit in well with a diagnosis of parapsoriasis but is a common finding in the earlier phases of mycosis fungoides.

DR. JAMES R. DRIVER: The lesions, particularly the larger plaques, present a dull reddish color, not unlike the pigmentation seen in phenolphthalein eruptions. On being questioned, the patient stated that she frequently takes Hinkle's pills and ex-lax; so the possibility of a drug eruption should be kept in mind.

DR. H. G. MISKJIAN: Brocq called attention to the fact that in some of these cases mycosis fungoides eventually develops. At present a diagnosis of psoriasiform parakeratosis of Brocq seems to me to be more nearly correct.

Tertiary Syphilis: Gumma of the Soft Palate, Interstitial Sclerosis of the Testicle, Asymptomatic Cerebrospinal Syphilis and Aortitis. Presented by DR. HAL ELSON FREEMAN.

F. C., a man aged 45, had a penile sore in 1919. His right testicle began enlarging in June 1939, and he first noticed an ulcer of the palate about September 1. He has lost 25 pounds (11.3 Kg.) in the past three months. He has never received treatment for syphilis.

There is generalized palpable lymphadenopathy. An irregular, reddish blue ulceration with a necrotic base is located on the right side of the soft palate, about 2 cm. in diameter. The right testicle is firm and painless and is the size of a goose egg, measuring $10\frac{1}{2}$ inches (27 cm.) in circumference. Light is not transmitted. The seminal vesicle is palpable and feels normal.

The heart was not enlarged, but there were systolic and diastolic aortic murmurs audible over the second right intercostal interspace. The pulse was of the Corrigan type. Pistol shot femoral reflexes and Duroziez' sign were present. The blood pressure was 140 systolic and 68 diastolic. The reflexes were normal.

The Wassermann and Kline reactions of the blood were strongly positive. The Wassermann reaction of the spinal fluid was strongly positive in all dilutions, the cell count was 13 per cubic millimeter, the reaction for globulin was positive, and the gum mastic test showed a reading of 3421100000. Roentgenograms and fluoroscopic examination of the chest showed the heart to be normal but there was enlargement of the aorta, with no evidence of parenchymal infiltration.

Histologic examination of tissue taken from the lesion on the palate showed moderate acanthosis, with elongation of the rete pegs. The upper part of the corium presented a diffuse, loosely arranged, cellular infiltrate composed of small round cells, fibroblasts and a few eosinophils. There were many newly formed and enlarged blood vessels. In the deeper part of the corium there was a heavy cellular infiltrate, granulomatous in character, and there were several areas of focal collection of epithelioid cells, small round cells, fibroblasts and newly formed blood vessels, with a few Langhans type giant cells to be found in one section. Deeper in the corium the collagen bundles were compressed and split by the infiltrate, and many blood vessels showed hyaline degeneration, with epithelioid cell infiltration in their walls and epithelioid and small round cell infiltrations perivascularly.

DISCUSSION

DR HAL ELSON FREEMAN. This patient was presented because of the rarity of gumma, syphilis of the central nervous system and cardiovascular syphilis in the same patient. There are two kinds of syphilis of the testicle, the gummatous form, which is soft, and the interstitial sclerotic form, which is firm and painless. In dealing with either it is well to remember that transillumination due to an associated hydrocele may be present.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILOLOGY

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Feb 6, 1940

A Case for Diagnosis (Papulonecrotic Tuberculid? Lupus Erythematosus?) Presented by DR FRANK VERO

F D, a girl aged 17, born in the United States, is presented from the Vanderbilt Clinic, complaining of a recurrent eruption of two years' duration on the hands and feet. There was no history of any previous disease of the skin. She had always been in good health except for attacks of tonsillitis. Tonsillectomy was performed five years ago. During infancy a gland was removed from her neck. For two summers the patient has had a recurrent eruption on the face, which has cleared up at the end of the season. An eruption appeared on the hands and feet a year ago, persisted during the winter and recurred four months ago.

Physical examination shows no abnormalities except on the skin. Examination on Dec 14, 1939 showed on the palmar surfaces of the fingers and hands, on the soles and on the face numerous peanut-sized to pea-sized, solitary and confluent,

violaceous, slightly infiltrated, papular, scaly lesions. In some areas there were small atrophic depressions. Some of the lesions felt dry, rough and keratotic. During the past four weeks several lesions have undergone spontaneous involution, but new lesions have appeared on the soles, especially on the inner aspect.

A roentgenogram of the chest, in the posteroanterior projection, showed no evidence of recent parenchymal infiltration or consolidation. Both lung fields were clear. The costophrenic angles were clear. The cardiac contour was not unusual, and the trachea was in the midline. A small shadow of calcium density was seen in the region of the left hilus. The Kline test gave negative results. The urine was normal. The blood sedimentation rate was 16 mm. in the first hour. The blood count showed 87 per cent hemoglobin and 4,300,000 erythrocytes and 6,200 leukocytes per cubic millimeter, with a differential count of 40 per cent polymorphonuclear leukocytes, 49 per cent small lymphocytes and 5 per cent large lymphocytes, 3 per cent monocytes and 3 per cent eosinophils. There was a thick keratin layer which were small. The capillaries were dilated. There was no evidence of papulonecrotic tuberculid, but the histologic examination showed edema and infiltration, with mononuclear cells with parakeratosis. There was no evidence of papulonecrotic tuberculid, but the histologic picture suggested lupus erythematosus.

DISCUSSION

DR. JOSEPH J. ELLER: I think this case is one of lupus erythematosus disseminatus. The lesions on the hands are the type of this disease which sometimes resembles erythema multiforme.

DR. DAVID BLOOM: The lesions on the mucous membranes of the cheeks and on the palate favor the diagnosis of lupus erythematosus rather than that of papulonecrotic tuberculid.

DR. FRANK VERO: When this girl was seen in early December the lesions had a different clinical appearance. They were violaceous and grouped. Many of the lesions have undergone involution without any therapy. She was seen on several occasions during January and did not come back to the clinic until a few days ago. She never had any lesions on the eyelids until tonight. I could not detect any active lesions in the mouth, but she had a peculiar folding of the mucous membrane of the hard palate.

A Case for Diagnosis (Necrobiosis Lipoidica?). Presented by DR. ROBERT R. M. McLAUGHLIN (by invitation).

T. B., a woman aged 40, is presented from the Vanderbilt Clinic, complaining of an eruption on the legs of two years' duration. The lesions on the lower portion of the legs begin as tender subcutaneous nodules. These sometimes resolve, but some have broken down to form ulcers which have healed, leaving atrophic areas. Some of these show yellow centers, with red puncta and a pinkish brown areola with telangiectases. The cutaneous lesions have been concurrent with pain in the knee and ankle joints. The patient states that she has noticed the nodules since 1923. Injections of staphylococcus toxoid used in the treatment of blepharitis have seemed to aggravate the condition on the legs. The urine was normal. Tuberculin tests with old tuberculin gave negative results in a dilution of 1 to 100,000,000 and positive results in a dilution of 1 to 10,000,000. Treatment has consisted of ultraviolet irradiation since October 19, but the lesions are now progressive.

DISCUSSION

DR. JOSEPH J. ELLER: I am inclined to think this case is one of dermatitis artefacta.

DR. J. GARDNER HOPKINS: The lesions in their present stage look rather like necrobiosis lipoidica, though it is true that the history given by the patient and the extreme tenderness of which she complains do not fit this diagnosis.

DR E WILLIAM ABRAMOWITZ It may be of some importance to know that tests for sugar in the urine gave negative results

DR MAURICE J COSTELLO I agree with Dr Eller I think the eruption that this patient presents is dermatitis factitia The lesions are bizarre in shape, size, location and grouping It is true that they are symmetric, but I do not think that this is against the diagnosis of a self-induced eruption There is a loss of the pharyngeal reflex, and I think her whole make-up is of the hysterical type

DR DAVID BLOOM The lesions are dead white, and there is no yellowish tinge present I therefore suggest the diagnosis of morphea rather than that of necrobiosis lipoidica

DR ROBERT R M McLAUGHLIN (by invitation) It might be of interest to know that in 1930 this patient was considered to have hysteria This was not recorded on the history She was presented as possibly having necrobiosis, because when she was first seen in October the lesions were a great deal more yellow

A Case for Diagnosis (Mycosis Fungoides?) Presented by DR JAMES L MILLER (by invitation)

W O T, a housewife aged 58, is presented from the Vanderbilt Clinic, complaining of a generalized eruption of eight years' duration The eruption began as a round, half-dollar-sized plaque with dry scaling No complete remissions have occurred The lesions have improved somewhat, especially during the summer Itching has not been an outstanding symptom She has never had any systematized treatment until admission to Vanderbilt Clinic in October 1939 The patient has lost 40 pounds (18 Kg) in weight in the past three years but feels that this is due to a restricted diet (for financial reasons) No symptoms of any foci or infection exist except that she believes the remaining teeth are in poor condition The past history is not significant She had no serious illnesses except typhoid fever at the age of 18 She was born in this city and has always lived here She has had 9 children, 8 of whom are living and well, and three miscarriages Her mother died in childbirth, and her father is still alive and well at the age of 78 One sister had her arm amputated twenty-seven years ago for osteogenic sarcoma

Examination shows pea-sized to half-dollar-sized erythematous scaly plaques over the entire body with the exception of the palms and soles In places these plaques are definitely infiltrated, and on the forearms and thighs especially they are lichenified and not scaly In the scalp there are areas of normal skin between the plaques The face and ears, particularly the postauricular regions, are involved The nails are normal except for longitudinal striations on both thumbs and some yellowish thickening at the distal margins of the toe nails The left third toe nail is misshapen, thickened and blackened There are no distinct pits present The mucous membranes are not involved General physical examination gives negative results except for six lower teeth which are in poor condition There is a soft systolic murmur at the apex of the heart The blood pressure is 164 systolic and 80 diastolic The left leg has been swollen and edematous below the knee for the past three weeks

The urine was normal The Wasserman reaction of the blood was negative Chemical examination of the blood showed 27 mg of nonprotein nitrogen per hundred cubic centimeters A blood count showed 80 per cent hemoglobin and 3,920,000 erythrocytes and 4,700 leukocytes per cubic millimeter, with a differential count of 65 per cent polymorphonuclear leukocytes, 33 per cent lymphocytes and 3 per cent monocytes

Histologic examination of a specimen taken from the left buttock showed a verrucous epidermal proliferation, the surface of which was vesicular and crusted Numerous polymorphonuclear leukocytes were seen here and there Hyperkeratosis and parakeratosis were considerable Acanthosis was extreme and formed a reticular pattern A large number of comedo-like structures were noted Intense

edema and infiltration, consisting of numerous plasmacytes, were present. Many other types of mononuclear cells were distinguished. The infiltration was particularly well marked in the papillae and just beneath the epidermis; deeper in the epidermis it was mainly vascular.

Histologic examination of a specimen taken from the left forearm showed decided acanthosis. The rete pegs were greatly elongated and clubbed. Superficial vesiculation was present. Parakeratosis and edema were both marked. Collections of polymorphonuclear leukocytes were seen in the epidermis. The corium was edematous. The blood vessels had thickened walls, and about them was an infiltration of small mononuclear cells. A few polymorphonuclear leukocytes were seen in the papillary portion of the corium. This specimen definitely represented a psoriasiform dermatitis.

Treatment has consisted of fractional roentgenotherapy (100 r) to the entire body from October to December 1939.

DISCUSSION

DR. A. BENSON CANNON: When I saw the patient with Dr. Miller a few days ago, we both felt that she was suffering from mycosis fungoides. I cannot reconcile a diagnosis of psoriasis in this case with symptoms of generalized eruption of such long duration, manifested by nodules and gyrate lesions, many of which are covered with a crustlike scale and accompanied by a moderate degree of itching. The favorable response of the lesions to treatment with roentgen rays would also indicate mycosis fungoides. The entire skin over her body is infiltrated, and when the patient bends her body large folds of thickened skin show. I should disregard the histologic report, and I suggest that a nodule be removed for further study.

DR. JOSEPH J. ELLER: I agree with Dr. Cannon that this case is one of mycosis fungoides in the plaque stage.

DR. SAMUEL FELDMAN: I want to point out that the presence of nodules in this case would not indicate that the patient has mycosis fungoides. I had a patient in the Bronx Hospital who was admitted with generalized erythroderma of about six years' duration, referred as having mycosis fungoides. The patient stayed in the hospital for about a month. The erythroderma disappeared, the nodules disappeared and she became entirely well. I found no signs of mycosis fungoides, but clinically the patient looked exactly the same as the patient presented tonight.

DR. PAUL GROSS: Although I favor the diagnosis of mycosis fungoides, the fact that histologic examination of a verrucous nodular lesion on the left buttock of this patient showed only a psoriasiform picture and not the pronounced infiltration one would have expected is noteworthy.

DR. JAMES L. MILLER (by invitation): The patient does not complain of as much itching as one would suspect. However, I still feel that the condition is in all probability mycosis fungoides.

A Case for Diagnosis (Poikilodermatomyositis?). Presented by Dr. J. GARDNER HOPKINS and Dr. PAUL GROSS.

D. O., a woman aged 59, a retired editorial writer, is presented from the Vanderbilt Clinic, complaining of an eruption involving the face, neck and extremities, of one and one-half years' duration. The eruption began on the left arm as an oval patch and then spread to the neck and other parts of the body. The onset was associated with attacks of dizziness, nausea, vomiting and muscular weakness. The muscular weakness was so pronounced that the patient was confined to bed for three months. The symptoms have subsided, but there is a great deal of thickening of the skin and muscles of the arms and neck.

Examination shows an eruption of purplish patches on the face, especially about the nasolabial folds, forehead, ears and chin. On the neck and chest, following the cut-out area of her dress, is a diffused purple erythematous eruption. The skin appears somewhat thickened and coarse, and there are numerous small telangiectases scattered throughout these areas. A similar diffuse eruption is present on the extensor surface of the arms and forearms. In addition, there are numerous small keratotic papules superimposed on the eruption on the forearms. On the dorsa of the hands are bluish red streaks following the extensor tendons of the fingers, and over the joints these lesions are somewhat hyperkeratotic. There is a varying degree of scaliness on the neck and extremities. On both knees are circumscribed reddish brown scaly patches of about the size of a palm, and there are lesions on the posterior surface of the right thigh. The skin on these lesions appears somewhat wrinkled. There is almost complete alopecia of the scalp. Physical examination showed nothing abnormal except in the skin.

The blood count showed 84 per cent hemoglobin and 4,090,000 erythrocytes and 11,100 leukocytes per cubic millimeter, with a differential count of 75 per cent polymorphonuclear leukocytes, 14 per cent lymphocytes, 9 per cent monocytes and 2 per cent eosinophils. There were slight anisocytosis and polychromasia. The antistreptolysin titer was normal (50 units). The coproporphyrin content was somewhat high (0.088 mg) in the twenty-four hour specimen of urine. Urinalysis gave otherwise normal results. Gastric analysis showed total acids 2 on fasting, 4 on examination twenty minutes after administration of histamine and 4 on examination forty minutes after administration of histamine. Each examination showed free hydrochloric acid.

Histologic examination was made on specimens taken from the skin and from the triceps muscle of the right arm. The section of skin showed hyperkeratosis, with a well defined granular layer. The epidermis was atrophic, with loss of the rete pegs. There was edema involving the deeper layer of the epidermis and the upper portion of the corium. The corium just beneath the epidermis contained ectatic capillaries and was the site of a rather intense infiltration with mononuclear cells. Many of these appeared to be lymphocytes, but occasional eosinophils were noted. This infiltration was not uniform. The specimen of voluntary muscle tissue showed some muscle fibers which were paler than those ordinarily seen. Some appeared to be atrophic, and an occasional fiber contained clumped nuclei. Between many of the fibers there was an increase of mononuclear cells, and there was also slight perivascular infiltration with mononuclear cells.

The patient's weight is 92 pounds (41.5 Kg). Her temperature during hospitalization ranged from normal to 100.8 F. Since Nov. 19, 1939 she has been given vitamin B complex, particularly nicotinic acid up to 400 mg per day, injections of liver extract and riboflavin 10 mg per day. There have been an increase in appetite and an improvement of the general condition, with moderate gain in weight, but no definite improvement in the eruption has been noted.

DISCUSSION

DR LOUIS CHARGIN. I should like to see dermatomyositis and poikiloderma separated, as they are probably not one and the same disease. They are unlike clinically and histologically. It is true that dermatomyositis may in one or another of its stages present the aspects of poikiloderma, and this has given rise to the confusion. Dermatomyositis presents a degenerative process of the collagen, while poikiloderma presents a cellular infiltration in the cutis. If cases of these diseases are carefully studied from this standpoint, as well as from the clinical standpoint, one will find that the conditions are not identical.

DR PAUL GROSS. The patient was treated extensively with the vitamin B complex, but so far the response has not been satisfactory. Yet in another patient presented here a few months ago the injection of liver extract produced considerable improvement manifested by gain in weight and increased muscular strength. There has been no recurrence of myositis, and the condition of the skin has

remained satisfactory since this therapy has been instituted. I do not wish to imply, however, that vitamin B deficiency is an etiologic factor in dermatomyositis.

DR. J. GARDNER HOPKINS: When I first saw this patient, I admit I made a diagnosis of pellagra or some related dermatosis. The eruption and its distribution were much like those of pellagra, and while she did not have any lesions of the mucous membranes or gastrointestinal symptoms, there was plenty in the background of the patient to suggest the possibility of deficiency in her diet. I think I almost convinced even Dr. Gross for a little while that the cause might be something of that sort. However, nicotinic acid made her distinctly worse; at least, she got the tingling sensation that nicotinic acid gives many patients. I think, therefore, I was wrong in the first instance.

Dr. Gross has brought up the possibility of poikilodermatomyositis, and while the muscle changes at present are a little indefinite, I was much interested that when the specimen of skin was shown to Dr. Machacek without any clinical opinion, he said the condition might be a radiodermatitis. There was decided collagen degeneration in the upper part of the cutis, but the vessels were fairly well preserved with hyalin around the walls, as in a case I presented here last year (*ARCH. DERMAT. & SYPH.* 39:761 [April] 1939). I do not feel that one can make any absolute diagnosis in this case yet.

DR. E. WILLIAM ABRAMOWITZ: What struck me were the follicular keratotic lesions on the forearms. If I had seen those lesions alone, together with the distribution of the eruption on the backs of the hands, I would probably have thought of pityriasis rubra pilaris. I think the question of vitamin A deficiency might also be considered here in addition to vitamin B deficiency.

DR. EUGENE F. TRAUB: This case was most unusual for many reasons, not the least of which was the fact that the lesions all seemed to be in areas exposed to sunlight. I did not hear any comment by the presenters about their opinion as to the effect of sunlight in this case, and I should like to ask them to take up this point. The demarcation at the top of the dress and on the forearms is abrupt, and the location even on the area of the knee is in a spot where sunlight would readily strike; hence, despite the fact that the patient says she seldom exposes herself to the sun, it would seem that this factor cannot be lightly dismissed. Assuming that exposure to the sun is a factor in producing this eruption, I wonder what interpretation would be given by Dr. Hopkins and Dr. Gross or whether it would alter their opinion about the diagnosis.

DR. LOUIS CHARGIN: I too cannot see the picture of dermatomyositis in this case. I have seen but a few patients with this condition, and they were acutely ill; this patient is not. In those I have seen, the eruption did not begin on the arm but on the face, with a little swelling around the eyes and a slight amount of erythema, not deep but superficial, such as one sees in lupus erythematosus. The eruption then spread to the neck and then to other parts, such as the arms and legs, and was associated with great weakness and muscular changes. I admit that I have not seen all forms of dermatomyositis, and this may represent one of the types. One must make a diagnosis here on the history and the course of the disease, and while there are certainly some features of dermatomyositis present in this case, other features suggest other possibilities.

DR. A. BENSON CANNON: I feel as Dr. Chargin does in regard to the case. I should hesitate to make a diagnosis of dermatomyositis. I had an opportunity to see Dr. Gray's patient in London a number of years ago and to study the histologic sections of tissue removed, and there was no resemblance between his patient and the one presented tonight. This patient's condition is quite different from that of the 2 patients that I showed with dermatomyositis before this society a few years ago and from that of other patients that were exhibited at the San Francisco meeting of the American Dermatological Association two years ago. I can detect no infiltrated, nodular swellings in this patient, nor can I notice any loss of substance where lesions have been, symptoms that I would naturally expect

to find This case is also different from the case submitted at the last meeting of the American Medical Association by Dr Hazel, with a histologic study made by Dr Weidman (Hazel, O G *Poikiloderma Atrophicum Vasculare* Report of Case, *ARCH DERMAT & SYPH* 40 776 [Nov] 1939) With the location of the red, swollen skin over the exposed parts and the cornified, follicular papules over the extensor surfaces of the forearms and hands, I should think that Dr Traub's suggestion of a vitamin deficiency in which a hypersensitiveness to sunlight played a part might be the proper explanation of the patient's symptoms In some respects the lesions simulated acute lupus erythematosus I should certainly want to rule out that possibility

DR PAUL GROSS Dr Hopkins and I have observed 4 cases of poikilodermatomyositis, 2 of which have been previously presented before this Section (*ARCH DERMAT & SYPH* 39 761 [April] 1939, *ibid* 41 1187 [June] 1940) All the patients had the chronic form of the disease There is a striking resemblance in these cases as far as the distribution goes Besides the face (swelling of the eyelids), the cut-out area of the neck, elbows, knees and knuckles of the hands seem to be the most favored sites for the cutaneous eruption The myositis in the patient presented tonight is not pronounced, but the history of muscular weakness at the onset, the extreme tenderness of the muscles and Dr Machacek's observations on the section of muscle seem to favor the diagnosis as presented The cause of these eruptions remains obscure Sensitization to sunlight is suggested by the distribution of the eruption and the high coproporphyrin content in the urine Mechanical irritation, like stretching of the skin over the joints, may account for the other localization These localizations are also found in pellagra, yet the main feature of pellagra is the nicotinic acid deficiency

Dermatitis Medicamentosa (Arsphenamine) Presented by DR CHARLES W McNITT (by invitation)

E A, a man aged 36, is presented from the Vanderbilt Clinic, complaining of a generalized eruption of two years' duration Two years ago, after a diagnosis of neuralgia and rheumatism was made, the patient received eight to ten injections (probably of a gold compound) Shortly after this treatment, it was discovered that he had a positive Wassermann reaction, and he was given twelve injections each of a bismuth compound and arsphenamine Two months later a moderate eruption developed, and all treatments were discontinued Six months later administration of the arsenicals was started again but had to be stopped because of the eruption with severe itching He was given injections of calcium, but the eruption became worse, and the skin began to peel and became red and swollen, with a serous exudate The entire body was affected with the exception of the palms and soles His hair fell out almost completely, but the nails were not lost

Examination shows that the patient has lost much of the hair of the head, eyebrows, beard, axillas and pubic region, the remaining hair is short and bristly The nails are all present The skin of the entire body with the exception of the hands and feet is involved in a process representing the end result of the previously described exfoliative dermatitis There is a general bluish violet tinge to the skin, most evident across the upper part of the chest, with a reticulated mottled appearance, which in places is purplish and in others shows brownish hyperpigmentation There is evidence of atrophy of the skin, with wrinkling and fine networks of depressed areas Telangiectasia is present On the volar aspect of the forearms are linear, branched, violaceous areas with definite induration There is glossitis and atrophy of the tongue, especially of the anterior two thirds

In a spectrographic study of the skin gold and bismuth were not detected, but silver was present (0.0008 mg per gram of dried tissue, or 0.0003 mg per gram of tissue as received) The Wassermann reaction of the blood was negative in both alcoholic and cholesterol antigens The Kline test gave a negative result A blood count showed 106 per cent hemoglobin and 5,200,000 erythrocytes and

5,900 leukocytes per cubic millimeter, with a differential count of 69 per cent polymorphonuclear leukocytes, 28 per cent lymphocytes, 2 per cent monocytes and 1 per cent eosinophils. The determinations of arsenic were as follows: 0.055 mg. per hundred grams of dry blood, 0.10 mg. in the twenty-four hour specimen of urine and 0.008 mg. per hundred grams of dry skin. The coproporphyrin content of the twenty-four hour specimen of urine was 0.010 mg.

Histologic examination was not completed at the time of presentation.

NOTE.—Histologic examination later was reported as showing poikiloderma.

DISCUSSION

DR. CHARLES W. McNITT (by invitation): I should like to ask the members whether they will try to answer questions along three lines: Is atrophy such as this man presents likely to follow arsenical dermatitis? Is it more consistent with poikiloderma? Or does it represent the changes one might find after lichen planus? I mention this third condition largely because of an interesting history which Dr. Harris gave me this evening. Arsenical dermatitis seemed to be the most probable diagnosis from the history of a dermatitis directly following the administration of an arsenical. The red, exudative, painful, peeling skin is consistent with exfoliative dermatitis. There was loss of hair but no loss of nails. Poikiloderma was thought of, and Dr. Machacek told me tonight that that seemed to be the diagnosis which the histologic picture most closely resembled. In reference to the history of lichen planus given by Dr. Harris, I feel that the question of the possibility that the arsenic stirred it up is an interesting one.

DR. JOHN H. HARRIS (by invitation): This man was sent to my office two years ago by one of the insurance companies. At that time he had a papular eruption which was practically universal, reticulated and violaceous. I made a clinical diagnosis of lichen planus and took a biopsy specimen, which was examined by Dr. Fraser. He reported that histologic examination showed the microscopic structure of lichen planus. At that time the patient stated that the eruption followed an accident, and he was claiming compensation. It is a known fact that lichen planus does leave pigmentation and also scarring. While I have never seen such decided scarring and pigmentation following lichen planus as this man presents, it is my opinion that it is still possible and probable that the condition he presents tonight is a result of the former severe lichen planus which he had. I do not think the eruption he presents at this time is associated with any medicine he has been taking or was given.

DR. SAMUEL M. PECK: In most cases exfoliative dermatitis following arsenic medication does not result in a clinical picture such as this patient presents. The hair that is lost during the course of exfoliative dermatitis is in most instances accompanied by loss of nails. However, it is unusual for the hair not to grow back. The alopecia differs from that seen in alopecia areata, because there seems to be actual atrophy of the skin. The hyperpigmentation which persists after any severe cutaneous eruption is due to a deposit of melanin free in the tissues, not in chromatophores. This sort of pigmentation is a form of autotattooing which persists for a long time.

DR. HERMAN GOODMAN: Will Dr. Peck dilate on the difference between loss of hair in alopecia from arsenical dermatitis and that in alopecia areata of the universal type?

DR. SAMUEL M. PECK: In answer to Dr. Goodman, I take it that he agrees with me that in alopecia areata there is no scarring.

DR. HERMAN GOODMAN: There is no scarring after arsphenamine dermatitis either, as far as I know.

DR. A. BENSON CANNON: I have observed 7 such cases as this one and presented 2 before this section and the New York Dermatological Society (ARCH. DERMAT. & SYPH. 36:1297 [Dec.] 1937; 38:822 [Nov.] 1938). In 5 of the cases

the changes in the skin—atrophy, pigmentation, telangiectasia and alopecia—followed an arsphenamine dermatitis, while in the other 2 cases there was no history of taking arsphenamine but the patients had taken arsenic by mouth. In a case which Dr Karelitz had been studying, the patient carried a dead fetus for a year and a half. Dr Howard Fox presented a patient with similar atrophy and pigmentation of the skin before the New York Dermatological Society two or three years ago and presented the patient again last year and suggested the diagnosis of poikiloderma (*ARCH DERMAT & SYPH* 38 115 [July] 1938). This patient had taken arsenic. In all likelihood, I think one might find that arsenic is the cause of the changes in the skin of the patient who is presented tonight, and I believe he should be thoroughly investigated for arsenic retention.

DR MARIE KARELITZ (by invitation) The patient of mine whom Dr Cannon mentioned was operated on and has greatly improved since then. She still has the alopecia, but the skin is not as atrophic as it used to be. The hyperpigmentation has also decreased a great deal.

DR HERMAN GOODMAN Did all these patients have arsenic or arsphenamine, or did they have a bismuth compound in addition? In 1 case there was a question of whether arsenic or arsenic and bismuth led to the pigmentation.

DR A BENSON CANNON I cannot remember whether the patients had a preparation of a heavy metal in addition to the arsphenamine or not, but I presume that they did. In the 2 patients who received no arsphenamine but took arsenic by mouth for other purposes, there was no history of a heavy metal compound having been given.

DR DAVID BLOOM I feel that the alopecia which is associated with an arsphenamine dermatitis and persists for a long time and which, as in this case, may be permanent is due not to the effect of the arsenic on the skin but to that on the sympathetic nervous system. If I understood Dr Peck correctly, he expressed the same thought.

DR LOUIS CHARGIN I know that I have seen this type of pigmentation and this type of skin in patients who have been given and have been found sensitive to the trivalent arsenicals. I also know that I have not observed such a condition following lichen planus. It is not a common sequela of the organic arsenicals and does not occur from bismuth. I think it is a peculiar arsenical dermatitis, a type not associated with much exudation but rather with scaling. In time the hair will grow again and the pigmentation will disappear. It may take a year or two. I recall a recent case under my observation with pigmentation of this type following the taking of arsphenamine. When the acute inflammatory process subsided, the pigmentation lasted about a year and disappeared, leaving some atrophy of the skin. That patient also had alopecia of the type shown by the patient presented tonight and now has a full head of hair.

DR PAUL GROSS I wonder whether the telangiectasia and the alopecia could not be interpreted as vascular damage due to arsenic.

DR EUGENE F TRAUB To arrive at a conclusion as to causal relations in a case like this one has to take into consideration, naturally, all the symptoms presented by the patient, and I do not know of any condition except that due to the ingestion of arsenic, particularly the types used for the treatment of syphilis, that would account for such a picture. While this condition is not common, it does occasionally follow antisyphilitic treatment. I believe, therefore, since in this particular case no other single condition will account for all the changes shown, that it must be accepted as a case of dermatitis following arsenical treatment.

DR CHARLES WOLF Lichen planus is occasionally followed by atrophy, but one never sees generalized lichen planus followed by disseminated atrophy, as in this case. There must be a secondary factor to produce this particular sequela. There is a possibility that the sympathetic nervous system may have played a role as suggested by Dr Bloom. The arsenical which was given to this patient

at a later date might have attacked the nervous system, with the consequence of producing this atrophy or pseudoatrophy and destruction of hair follicles.

DR. E. WILLIAM ABRAMOWITZ: I thought that this patient might well have all the symptoms he presents tonight from the arsphenamine medication. Poikiloderma-like changes have been reported by Grutz and others (Poikilodermeiartiger Folgezustand nach universeller Salvarsandermitis, *Zentralbl. f. Haut- u. Geschlechtskr.* 36:722 [April 5] 1931) as following a dermatitis due to arsphenamine. An unusual feature in this case is the glossitis. All forms of stomatitis are rather uncommon with arsphenamine reactions. Also, keratosis of the palms and soles, so characteristic of arsphenamine eruptions, is absent. He presents two keratotic lesions on the trunk, which are probably arsenical keratoses.

A Case for Diagnosis (Morphea? Lichen Sclerosus et Atrophicus of Hallopeau?). Presented by DR. PAUL GROSS.

W. N., a dock builder aged 57, presented from the Hospital for Joint Diseases, complains of an eruption on both legs of two and one-half years' duration. About four years ago osteoarthritis of both hips was diagnosed, and it was also found that he had a moderate degree of general arteriosclerosis. Neurologic examination gave negative results. He complained of a burning sensation in both legs.

Examination shows on the outer surface of both legs irregularly shaped, up to palm-sized patches in which the skin appears whiter, thin and somewhat wrinkled. In some places the follicles seem to be slightly enlarged. On the periphery there is a slightly erythematous zone but no typical lilac ring.

Histologic examination by Dr. Machacek showed hyperkeratosis, with some follicular plugging and atrophy of the epidermis, with loss of rete pegs. The corium just beneath the epidermis showed a pale glassiness. Fine fibrils were present. The superficial capillaries were dilated, and there was a focal perivascular infiltration of lymphocytes. Spindle-shaped cells were increased. In the glassy, finely fibrillar area there was a diminution or absence of elastic fibers. The histologic picture was compatible with the diagnosis of lichen sclerosus et atrophicus.

Lichen Sclerosus et Atrophicus. Presented by DR. RICHARD J. KELLY.

A. M. R., a girl aged 17, is presented for Dr. Bazemore from the Vanderbilt Clinic. She has had an eruption for nine months which involves the posterior surface of the right wrist, the area over the sternum, the left side of the neck and the left ankle. The lesions are irregular in outline, atrophic and of a peculiar whitish color. In the centers horny plugs can be seen.

Histologic examination on Aug. 8, 1939 showed that although the section represented a superficial portion of skin, the changes in the skin appeared to be those which occur in cases of lichen sclerosus et atrophicus.

Treatment has consisted of superficial desiccation at intervals of two weeks.

Lichen Sclerosus et Atrophicus. Presented by DR. RICHARD J. KELLY.

R. S., a woman aged 50, is presented for Dr. Bazemore from the Vanderbilt Clinic. On admission to the clinic on June 21, 1938 she complained of an eruption on the neck and shoulder of one year's duration. The lesions were irregular in outline and were composed of atrophic white papules, which were surrounded by a narrow erythematous area. The serologic tests for syphilis gave negative results. Histologic examination showed typical changes seen in cases of lichen sclerosus et atrophicus.

On October 7 treatment was begun with superficial desiccation at intervals of two weeks. The patient has improved greatly. There is much normal epithelium at the sites of the old lesions.

DISCUSSION ON CASES OF LICHEN SCLEROSUS ET ATROPHICUS

DR DAVID BLOOM The result of the treatment in these cases seems to me cosmetically better than that which I have observed from spontaneous involution of the lesions

DR E WILLIAM ABRAMOWITZ Is the diagnosis accepted? One of the patients, a woman, I believe was seen at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital some time ago. She presented lesions on the back of the trunk. The result of desiccation of the lesion is excellent.

DR PAUL GROSS The case shown by me is presented for diagnosis.

DR BAZEMORE (by invitation) The histologic diagnosis for the third patient by Dr Machacek was lichen sclerosus et atrophicus. I started treatment with desiccation every two weeks for about six months and then every three weeks. For the past six months I have just been following her, without further treatment.

A Case for Diagnosis (Dermatolysis?) Presented by DR BEATRICE M KESTEN

Miss M, aged 27, is presented from the Vanderbilt Clinic, complaining of an eruption involving the neck, wrists, chest and abdomen of six years' duration. After loss in weight of 20 pounds (9 Kg), the patient noticed that the skin in the aforementioned areas became lax, easily stretched and wrinkled. The condition has remained about the same since then, with no symptoms except possibly slight dryness. She has used various creams to soften the skin but has noticed no change.

The Wassermann reaction was negative. The basal metabolic rate was —7 per cent. The urine was normal. A blood count showed 90 per cent hemoglobin and 4,930,000 erythrocytes and 7,600 leukocytes per cubic millimeter, with a differential count of 77 per cent polymorphonuclear leukocytes, 12 per cent small lymphocytes, 4 per cent large lymphocytes, 7 per cent monocytes and no basophils or eosinophils. Chemical examination of the blood showed 88 mg sugar, 24 mg nonprotein nitrogen, 33 mg uric acid, 11 mg urea nitrogen and 180 mg cholesterol per hundred cubic centimeters.

The histologic diagnosis was dermatolysis (aplasia of the elastic tissue). The epidermal changes were not striking. Superficial vessels showed an increase of perivascular cells. Sections stained for elastic tissue (with orcein) showed the development of elastic tissue to be sparse. This was most evident in the deeper part of the corium, where elastic tissue was seen only in localized foci.

DISCUSSION

DR HERMAN GOODMAN This patient looks much like one whom the late Dr Clarke showed twenty years ago with a diagnosis of pseudo xanthoma elasticum (*ARCH DERMAT & SYPH* 4 419 [Oct] 1921). Was there elastorhexis or a jumbling of the elastic tissue in small clumps? Three or 4 cases were reported many years ago. I recall that there was a diamond-shaped clearage in the creases unlike the wrinkling in old age. This patient showed such formation. Each diamond had a slight protrusion, and it was a little bit off color. The lesions in the axilla have been described previously. Some years ago Jones, Alden and Bishop (*ARCH DERMAT & SYPH* 27 424 [March] 1933) reported similar cases in which there were likewise streaks in the retina. It might be well to make an examination in this case to prove the presence or absence of these retinal streaks.

DR J GARDNER HOPKINS It did not seem to me that this patient showed the yellow color of pseudo xanthoma. I remember the histologic section. It showed no clumping of elastic tissue but a loss of elastic tissue.

DR G F MACHACEK The biopsy specimen was taken from the abdomen, as I remember. There were a sparseness and fragmentation of the elastic tissue rather

than the clumping ordinarily seen and considered to be typical of pseudoxanthoma. However, if I remember correctly, no biopsy specimen was taken from the neck.

DR. GEORGE C. ANDREWS: I happen to remember the case mentioned by Dr. Goodman. I do not see any reason for classifying it as one of pseudoxanthoma, as it is a classic case of dermatolysis or cutis laxa.

DR. E. WILLIAM ABRAMOWITZ: I recall a report (Frost, K.: *Pseudoatrophoderma Colli in Sisters*, ARCH. DERMAT. & SYPH. 40:755 [Nov.] 1939) in which the lesions described bear a close resemblance to those in the case presented tonight.

DR. MARION B. SULZBERGER: In this case I think it is possible that the patient may have a partial Ehlers-Danlos syndrome. The skin is elastic everywhere and is stretchable but not lax. There is a peculiar, soft, velvety feeling to the skin which is characteristic, I think, of those cases. I should like to ask Dr. Machacek if the histologic observations would be in consonance with that diagnosis.

DR. G. F. MACHACEK: I can only say that the histologic picture fitted in with the changes known as dermatolysis. There was a loss of elastic tissue, or at least fragmentation, and I think that accounts for the looseness and peculiar texture of the skin. There is no elasticity, in spite of the looseness of the skin.

DR. J. GARDNER HOPKINS: My impression was that these two conditions are rather the converse of each other. With the Ehlers-Danlos syndrome the skin is hyperelastic and shows an excess of elastic tissue, while with dermatolysis the skin loses its elasticity and the elastic fibers are diminished.

DR. DAVID BLOOM: On clinical grounds I would diagnose this case as one of pseudoxanthoma elasticum.

DR. EUGENE F. TRAUB: From a single inspection of this patient, it is practically impossible to arrive at a clinical diagnosis, but I doubt that several of the conditions mentioned should be considered. The case certainly does not seem to me to be one of pseudo xanthoma elasticum, which I do not believe as a rule is so widespread a condition as that presented by the patient tonight. The diagnosis of dermatolysis made by Dr. Machacek on the examination of the removed tissue may explain some of the changes, but I believe the case has to be studied further and should be reported again.

DR. BEATRICE M. KESTEN: I am afraid the condition in this case will have to be considered a symmetric loss of elastic tissue of the skin, both clinically and histologically.

Scleroderma with Secondary Unilateral Muscular Atrophy. Presented by DR. ROBERT R. M. McLAUGHLIN (by invitation).

J. C., a man aged 55, is presented from St. Luke's Hospital, complaining of an eruption of fourteen years' duration on the left leg and left arm. The onset followed high voltage roentgenotherapy for pains in the ankle and knee. The patient received ten treatments, the last one being fourteen years ago. The pains in the joints disappeared, but the muscles of the leg have slowly atrophied to their present size. The skin was at first reddened along the anterior surface of the shin and became thickened and glazed. About the same time the cordlike lesion of the skin on the outer aspect of the left arm appeared. At times the lesions have been painful.

Examination shows on the left leg an elongated thickened mottled area, with a smooth waxy surface. The central portions are ivory yellow. They are surrounded by peripheral discoloration that appears to be pigmentation. The cordlike lesion on the left arm is covered with similar smooth, glazed, yellow skin. The feet show clinical dermatophytosis and recurrent cyanosis of the great toes.

The urine was normal. Chemical examination of the blood showed 147 mg urea nitrogen, 110 mg sugar, 52 mg chlorides, 11.5 mg calcium and 175 mg cholesterol per hundred cubic centimeters. Examination of the urine for arsenic gave negative results.

DISCUSSION

DR CHARLES WOLF: I do not know whether Dr McLaughlin intended to suggest that the atrophy was a result of roentgenotherapy. If he did, I should like to give my viewpoint on that particular question. Scleroderma has been treated with roentgen rays on many occasions, with varying results. Cases have been observed for years, and no atrophy of muscles has resulted from the administration of the roentgen rays. Furthermore, roentgen rays are being used in tremendous doses every day and have been for the past fifteen to twenty years, with high, low and intermediate voltages, and at no time, especially in cases of cancer of the larynx, in which the doses given are tremendous, has anything that resembles atrophy of the muscles occurred. I think, therefore, it is far fetched to attribute muscular atrophy in this case to roentgenotherapy.

DR ROBERT R. M. McLAUGHLIN (by invitation): I should like to clear up some points. When the patient arrived here he was recognized by some of the members who treated him at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, I believe, about eight years ago. He did receive some roentgenotherapy at that time for the cutaneous lesions. I really think his condition is scleroderma associated with or preceded by pains in the joints and followed by muscular atrophy. There is atrophy of the muscles of the left arm where he did not receive any roentgenotherapy. The whole condition is unilateral, involving the left side of the body. The patient has a fixed idea that the atrophy of the muscles is due to the roentgenotherapy that he received fifteen years ago.

A Case for Diagnosis (Granuloma Annulare? Papulonecrotic Tuberculid?)

Presented by DR E. WILLIAM ABRAMOWITZ

Y. F., a woman aged 43, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complaining of an eruption on the back, shoulders, chest and arms of three years' duration.

The aforementioned areas show pinhead-sized to pea-sized, elevated, bluish red papules, some having slight umbilication and others forming rings. Some of the lesions show follicular, crusted plugs, and some are pustular.¹ On the arms and legs there are discrete, similar lesions, some showing definite necrosis. On the lower part of the back there is extensive macular atrophy.

The Wassermann and Kahn reactions were negative. Tuberculin tests showed the following results: 1 plus with a dilution of 1 to 1,000,000, 2 plus with a dilution of 1 to 100,000 and 4 plus with a dilution of 1 to 10,000. Histologic examination showed the "structure of granuloma annulare."

DISCUSSION

DR MAURICE J. COSTELLO: I believe Dr Morse described a case six or seven years ago (Morse, J. L. Lichenoid Sarcoid [Boeck], *New York State J. Med.* 33: 686 [June 1] 1933) which might apply to this one. It was described as a case of lichenoid sarcoid.

DR DAVID BLOOM: The decided hypersensitivity to tuberculin is more in favor of the diagnosis of papulonecrotic tuberculid than of that of granuloma annulare or sarcoid.

DR E. WILLIAM ABRAMOWITZ: This condition is microscopically granuloma annulare. I added the diagnosis of papulonecrotic tuberculid because of the fact that the lesions on the elbows and knees resembled that disease more than any other, whereas the lesions on the back in some instances had the appearance of granuloma annulare but in other instances did not. Some of them had more the appearance of sarcoid.

Tuberculid with Rosacea-Like Manifestations. Presented by DR. G. F. MACHACEK.

A. S., a woman aged 32, is presented for Dr. Bazemore, from the Vanderbilt Clinic, complaining of an eruption on the face and neck of twenty-eight months' duration. The lesions are erythematous and papular, with some superficial scarring and some depressions. On admission the lesions were widespread, located on the forehead, cheeks, chin and neck, and were of such intensity that they gave the impression of being a contact dermatitis.

The histologic report on April 5, 1938 was that of typical tuberculid. A roentgenogram of the chest on April 11 showed calcified apical shadows, interpreted as healed minimal tuberculosis. On admission the patient reacted to tuberculin in a dilution of 1 to 100,000 (reaction of 3 cm.).

Treatment was started with tuberculin in a dilution of 1 to 10,000,000, with a weekly increase of 0.1 cc. During the treatment she has slowly improved. She has reacted from time to time with dilutions as high as 1 to 100,000,000. For the past six months she has been given 0.1 cc. of a 1 to 10,000,000 dilution. From this dilution she has had infrequent reactions that were followed by definite improvement. The reason for the diminished dosage was the occurrence of reactions of increasing severity.

Tuberculid with Rosacea-Like Manifestations. Presented by DR. G. F. MACHACEK.

E. P., a woman aged 31, is presented for Dr. Bazemore, from the Vanderbilt Clinic, complaining of an eruption on the face for four years and nine months. The lesions are erythematous, papular and pustular, with some scarring.

A roentgenogram of the chest on May 18, 1939 showed a few small shadows of calcium in the left hilus. Bronchovascular markings were somewhat exaggerated. The condition was interpreted as minimal healed tuberculosis. Histologic examination on April 6, 1938 showed cystic comedones surrounded by tuberculid granuloma.

On admission the patient was sensitive to old tuberculin in a dilution of 1 to 10,000,000, with a reaction of 3 cm. in diameter. Treatment was started with old tuberculin in a dilution of 1 to 1,000,000,000, beginning with 0.1 cc. and increasing the dose 0.1 cc. a week. It was found that the sensitivity changed. When reactions occurred the eruption tended to clear. The eruption has cleared on numerous occasions but has recurred. Three weeks ago the patient states she had a "cold." At this time the eruption recurred. Since then it has responded to treatment.

Tuberculid with Rosacea-Like Manifestations. Presented by DR. G. F. MACHACEK.

F. C., a woman aged 29, is presented for Dr. Bazemore from the Vanderbilt Clinic, complaining of an eruption on the face of five and one-half months' duration from its onset to the time that it cleared up under treatment. The lesions were erythematous, papular and pustular.

A roentgenogram of the chest on June 29, 1939 showed minimal healed tuberculosis. Histologic examination on May 18 showed typical tuberculid, composed of tiny epithelioid tubercles. On admission to the clinic the patient was sensitive to old tuberculin in a dilution of 1 to 100,000 (reaction 6 cm. in diameter). The following week she had a reaction to a dilution of 1 to 1,000,000.

Treatment consisted of injections of old tuberculin, in a dilution of 1 to 100,000,000, 0.1 cc. once a week. After five weeks she had a reaction, and the lesions cleared. She was given a vacation for two weeks, and the lesions recurred. Treatment was continued, and she had reactions weekly for four weeks, after which the lesions cleared a second time. After this she was given four more injections. Since that time (Oct. 26, 1939) she has been observed and her face has been clear.

DISCUSSION ON CASES OF TUBERCULID WITH ROSACEA-LIKE MANIFESTATIONS

DR BAZEMORE (by invitation) I have been following these cases for the past two years. Histologic examination of tissue from 1 patient showed small epithelioid tubercles. After she had a reaction to the old tuberculin, the lesions cleared rapidly. I noticed this in the other 2 cases also. In the third case I did not know exactly when to stop treatment, and the patient returned in two weeks with a recurrence. I treated her four weeks longer until she cleared up and then continued treatment once a week for another month. As for the other cases, I do not know whether the infiltrated lesion in the 1 case should be called rosacea-like tuberculid or lupus miliaris disseminatus faciei. It belongs in one of those two groups. The condition is progressively getting better, but the improvement has been a slow process. The patient with the acute eruption at present has been treated in the same way. Every time she gets an acute reaction, there is a tendency for the lesions to clear up quickly.

DR MARION B SULZBERGER As far as one can determine on inspection alone, the 2 cases in which lesions still show tonight seem to be examples of rosacea-like tuberculid. The additional evidence Dr Machacek has brought out confirms that diagnosis based on clinical inspection. I think the hypersensitivity to tuberculin, which in these cases was extreme, is certainly in favor of that diagnosis. The majority, at least, of patients with lupus miliaris disseminatus faciei are hypersensitive to tuberculin, i. e., are even less sensitive than the majority of normal persons. I do not believe the fact that the tubercles in 1 case were larger than in the other is against rosacea-like tuberculid. However, I think if one found histologic evidence of caseation, that would be against that diagnosis. I believe that these cases are of practical importance, and that such conditions are not at all uncommon and are often erroneously diagnosed as rosacea or acne. They are observed in private and in clinical practice with a fair degree of regularity and seem to be more common in women. Dr MacKee and I had similarly good results from the intracutaneous injection of old tuberculin in some patients with these eruptions (*ARCH DERMAT & SYPH* 31 159 [Feb] 1935). Were any of these patients first given the orthodox treatment for rosacea? If so, how did they respond? I should also like to know what tuberculin was used. Was it old tuberculin from the board of health?

DR E WILLIAM ABRAMOWITZ Is treatment with tuberculin more effective and safer than treatment with a gold compound would be? After all, these patients have some old healed foci, usually in the chest.

DR EUGENE F TRAUB Speaking of therapy in a small group of cases, possibly 5 or 6, I have had excellent results with small doses of ultraviolet radiation or with irradiation from a quartz mercury vapor glow lamp, together with white lotion N F. All of the patients had a positive diagnosis that was based on removed sections of skin, and all the conditions cleared up in less than six months. Two or three that I was able to follow for several years remained entirely well, without new lesions. This type of treatment is absolutely foolproof and devoid of any danger of reaction, as might be expected from any type of injection.

DR LEWIS B ROBINSON I presented 1 of these cases a year ago, and at that time Dr Sulzberger did not accept the diagnosis of rosacea-like tuberculid.

DR CHARLES W McNITT (by invitation) I should like to have a little more information about the technic of the injections. How does one decide what dilution to use? Do the patients get any flare-up of the lesions on the face? Is it a local or a focal reaction? Do the physicians judge the effect by the local reaction in the skin?

DR BAZEMORE (by invitation) Only 1 of these patients had had previous treatment. She had treatment with white lotion N F, salicylic acid and other medicaments. The others had no treatment whatsoever. The old tuberculin

I used is that obtained from the board of health. As for technic, I have made it a rule to start off by making cutaneous tests of these patients with a dilution of 1 to 100,000,000. If there is no reaction in four or five days, the test is made with a dilution of 1 to 10,000,000, and the dilution is decreased until a reaction is obtained. If the patients react to a dilution of 1 to 1,000,000, I go back to the dilution of 1 to 10,000,000 and give 0.1 cc., increasing the dose 0.1 cc. a week.

DR. JOSEPH J. ELLER: I have had several cases of this type in which the condition did not respond to the ordinary treatment for acne rosacea but did respond satisfactorily to the gold therapy. I should like to hear from other members who have had good results also from gold therapy and should like to know whether the results with tuberculin were just as good or better than with a gold compound. I agree with Dr. Abramowitz that there is a possibility of danger in giving injections of tuberculin to a patient with latent tuberculosis and wonder if use of gold compounds is not a safer form of treatment.

DR. MARION B. SULZBERGER: I have had relatively little experience with patients with rosacea-like tuberculid treated either with a gold compound or with tuberculin, as my total number does not exceed 15, but I have, of course, had sufficient experience with both substances in the treatment of other conditions. The only unpleasant sequelae I have seen have been with a gold compound. For example, I had 1 patient nearly die after injection of 25 mg. of gold sodium thiosulfate. I have seen no flare-ups with the tuberculin treatment except of the cutaneous foci. In treating tuberculoderms with tuberculin, one not uncommonly produces focal reactions in or around the cutaneous lesions, and these focal reactions sometimes seem to exert a beneficial effect. I have, of course, always examined patients thoroughly before starting tuberculin desensitization and have never instituted this treatment in patients with suspected or actual active foci in the lungs or other vital organs. I have used tuberculin only in patients with healed, i. e., calcified, lesions in the lungs. I suspect that it would be relatively safe to use the proper technic of tuberculin desensitization even in a patient with active lesions in the lungs, but I do not know whether it would always be entirely safe to use a gold compound in such a case.

MANHATTAN DERMATOLOGIC SOCIETY

GEORGE C. ANDREWS, M.D., *President*

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Feb. 13, 1940

Branchial Cyst. Presented by DR. GEORGE C. ANDREWS.

F. B., a Negress aged 21, was referred to the dermatologic department from the medical division of Vanderbilt Clinic in November 1938 because the result of a routine Wassermann test was 4 plus.

A cystic lesion was noted above the right ear on Feb. 8, 1940 and was said to have been present for two months. The lesion was aspirated, and 0.5 cc. of yellow turbid fluid was obtained. No tenderness or inflammation was noted. The aspirated fluid is yellowish, honey colored, thin and watery. The upper part of the ear is tilted outward as a result of deformity of the cartilage. A bony depression is evident beneath the lesion. Antisymphilitic treatment had no effect on the lesion.

DISCUSSION

DR. ANDREW J. GILMOUR: The lesion is probably not a sebaceous cyst because it became so soft in such a short time. A sebaceous cyst stays fairly hard for a longer time. This might possibly be a gumma.

DR L P BARKER (by invitation) The fluid aspirated from the lesion is clear and straw colored and jells on standing I have never seen this type of fluid obtained from a sebaceous cyst Another interesting feature is that the bone of the skull beneath the cyst is depressed A surgeon in consultation agreed with the diagnosis of branchial cyst, probably of the first branchial cleft

Pyoderma Presented by DR GEORGE M LEWIS

J C, a girl aged 14, attended the New York Hospital for the two months before presentation Previously she was treated in another institution for acute meningitis and acute mastoiditis on the right side Later she was treated for hepatomegaly, splenomegaly and a superficial ulcer of the leg She made slow recovery after surgical and medical treatment The wound resulting from the mastoidectomy never completely healed When she was first observed at New York Hospital, there was a deep sluggish ulcer of the left leg with considerable undermining of the edges Pus could be expressed from all sides of the lesion There were also lesions of impetigo on the face and hands Cultures of material from the mastoid sinus and also from the ulcer of the leg revealed *Staphylococcus aureus* and nonhemolytic and beta hemolytic streptococci The hemogram was normal The Wassermann reaction was negative Cod liver oil and generalized ultraviolet radiation were given She received sulfanilamide on two occasions The ulcer healed considerably but still showed the same characteristics as noted on her first visit

DISCUSSION

DR MAURICE J COSTELLO I suggest that in addition to the administration of sulfanilamide, zinc peroxide paste be applied in the manner outlined by Dr Meleney He thinks that the results are superior when both medicaments are used together than when either is used alone The zinc peroxide is used to fill the wound, and the dressing is made as air tight as possible

DR ANDREW J GILMOUR I suggest that the patient have the lesion on the leg strapped with adhesive plaster, leaving only enough room for the secretion to escape I have done this and have also used a mild (10 per cent) mercurial ointment That seemed to work well How much improvement was due to the mercury and how much was due to the bandage I do not know, but the combination helped greatly

DR WILBERT SACHS I suggest that tuberculin tests be made, and if the results are negative, I favor a diagnosis of multiple sphaceloderma In these lesions all types of organisms may be found It is difficult to prove whether or not a certain organism is the responsible agent In the case that I reported, little seemed to help the patient, although everything was tried

DR DAVID BLOOM This case is one of gangrenous pyoderma As in other cases of this kind, there is a history of a previous debilitating illness From observation of several cases I have come to the conclusion that the main treatment should consist of increasing the resistance of the patient by all means possible, which should, of course, include a diet adequate in vitamins Local treatment is of minor importance

DR E WILLIAM ABRAMOWITZ I observed my first case of this type at the Jewish Memorial Hospital a few years ago A woman had colitis There was no doubt that a high caloric diet and plenty of vitamins caused the lesions to disappear Only a bland ointment was used locally The lesions recurred whenever she did not adhere to the diet This child had several infections which were enough to break down her general resistance I suggest that, irrespective of what local treatment is given, the child get plenty of vitamins and a high caloric diet

DR GEORGE M LEWIS This patient has been and still is a problem, and the chronic ulcerative lesion is a result of her lowered resistance

A Case for Diagnosis (Psoriasis Pustulosa? Dermatitis Exfoliativa?).

Presented by DR. E. WILLIAM ABRAMOWITZ.

J. R., aged 53, formerly a furrier, born in Austria, has been under my care since Aug. 14, 1933. He was subject to asthma in 1917 and had his gallbladder removed in 1930. He is in apparently good health except that he is constipated. The eruption first appeared on the toes and then spread to the rest of the body. It disappeared for three years and then reappeared on the hands and spread to the chin and ears. When he was seen in 1933 the eruption had extended to the rest of the body, with patches of crusted vesicles and scaly areas of dermatitis which had been present for two years. There was some scaling between the toes. Examination of the palmar vesicles for fungi gave negative results repeatedly except once. Since then the eruption has disappeared from the face and at times from the body. Vesicles and pustules have persisted on the palms. Extensive erythematiforme-like lesions have appeared on the trunk and the upper and lower extremities during the past three months; some of these lesions presented central pustules. The lesions on the body have receded somewhat, only to recur again during the past two weeks. There is considerable grooving of the finger nails. At present he has a profuse eruption of the body and face with exfoliation of the palms. His toes are clean, but vesicles are present on the soles. The original diagnosis of the lesions on the face was sycosis fungoides. Histologic examination in 1935 of a lesion on the right palm showed pustular psoriasis. Numerous laboratory examinations have been of little help. Cutaneous tests showed that he is sensitive to paraphenylenediamine. He has had innumerable types of treatment, with little benefit. He is presented for diagnosis and for suggestions as to treatment.

DISCUSSION

DR. ANTHONY C. CIPOLLARO: I cannot offer an unequivocal diagnosis. The eruption appears to be one of possible psoriasis, becoming generalized and finally developing into dermatitis exfoliativa psoriatica. The tongue is red, patchy and somewhat edematous. These signs suggest an infection with Monilia. If Monilia is found, I think this patient should be treated with inhalations of ethyl iodide.

DR. GEORGE M. LEWIS: The palmar lesions are typical of pustular psoriasis. Some of the lesions on the trunk and arms resemble seborrheic dermatitis. English physicians have stated the belief that psoriasis and seborrheic dermatitis are closely allied. Why could not this case be one of the transitional cases reported, in which from time to time the condition resembles one disease or the other? I have discontinued using ethyl iodide, as my results were disappointing. I could not establish that there was any more benefit from ethyl iodide given by inhalation than from potassium iodide given orally. Furthermore, in certain instances toxic effects led to discontinuing its use. Perhaps Dr. Cipollaro will tell why he advocates its use.

DR. ANTHONY C. CIPOLLARO: The little experience which I have had with ethyl iodide convinces me that there are certain cases of fungous infection in which this method of treatment is of value. It is of value especially for extensive fungous infection which is recalcitrant to ordinary methods of treatment. I do not advocate inhalations of ethyl iodide in ordinary cases of dermatophytosis.

DR. DAVID BLOOM: I am unable to make a definite diagnosis of pustular psoriasis of the palms in this case. However, this condition may at times assume an aspect which is not typical of pustular psoriasis. This diagnosis can therefore not be excluded definitely.

DR. E. WILLIAM ABRAMOWITZ: I should like to review what happened in this case. The eruption started with a vegetative type of sycosis, which finally cleared up with chlorhydroxyquinoline ointment. The patient had lesions on the body at times which reminded me of psoriasis. For a long time he had only the palmar eruption, which consisted of dry vesiculopustules, sometimes becoming necrotic in the center, suggesting papulonecrotic tuberculids. During the last few months

he had one attack similar to the present, a condition resembling toxic erythema. At that time he had a few alcoholic drinks. This time he had twelve or more drinks, two days later this generalized eruption appeared again. He has bad teeth. He had to stop working as a furrier for he found the handling of furs caused an aggravation of the eruption on his hands. The histologic examination suggested pustular psoriasis. Whether he has in addition to the pustular psoriasis a coincidental toxic eruption of some kind or an exfoliative psoriasis is still a question.

Erythema ab Igne Presented by DR MAURICE J COSTELLO

E J, a married white woman aged 32, from Bellevue Hospital, had a genital syphilitic chancre in 1932, which was followed by a secondary eruption. At that time she had inadequate antisyphilitic treatment. On the upper third of the posteromedial aspect of the left thigh there is a dark brown reticulated eruption which appears to correspond roughly with the network of the superficial veins. There are a few superficial crusts on the noninfiltrated pigmented areas, and there is atrophy. The affected area corresponds to that part of the left thigh which came in contact with a heated radiator which the patient sat on. The patient was not aware of the presence of the eruption until three weeks ago. The right thigh is not similarly involved because she crossed the right leg over the left.

The Wassermann reaction of the blood was negative three times in the past three weeks. The case is presented because the condition simulates a diffuse tertiary syphilid.

Erythema Annulare Centrifugum Presented by DR E WILLIAM ABRAMOWITZ

V R, a woman aged 31, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital with an eruption on her right thigh, which had been recurring since 1933. The present attack began two months ago. Previous to this she had been free of cutaneous lesions for four years.

The patient presents annular, erythematous, elevated, somewhat scaly lesions, tending to group, with clearing in the central portions, on the left thigh. A few smaller lesions are present on the body and arms.

She has been receiving ultraviolet therapy since December 1939. The histologic picture suggested erythema annulare centrifugum.

DISCUSSION

DR WILBERT SACHS: It is interesting to note that in many cases like this some one suggests the possibility of pityriasis rosea. Last year Dr Lewis and I had a case in which the possibility of pityriasis rosea also was considered.

DR GEORGE M LEWIS: In this case there is no clinical evidence of tinea of the feet or nails. This fact and the more evanescent type of lesion tend to rule out the diagnosis of infection due to *Trichophyton purpureum*, which sometimes simulates erythema annulare centrifugum.

DR E WILLIAM ABRAMOWITZ: This is the third example of the disease that I have seen in women of approximately the same age and with circular lesions of the same distribution. The eruption disappeared in the others after ultraviolet irradiation but recurred.

A Case for Diagnosis (Epithelioma [Flat Basal Cell? Bowen's Disease?]) Presented by DR GEORGE M LEWIS

K F, a housewife aged 30, when examined at the New York Hospital stated that she first noticed a small red scaly lesion on the left side of the back two years ago. There was a gradual increase in its size, but it did not change in character. The condition had been treated as eczema by two local physicians. On

the left side of the back below the level of the tenth rib was an irregular dull red plaque with an elevated border. The surface showed some fine scaling. The central portion of the lesion appeared atrophic.

DISCUSSION

DR. MAURICE J. COSTELLO: I think this condition is a superficial type of basal cell epithelioma because of the definite raised, threadlike, pearly border.

DR. MAX SCHEER: This condition is a superficial erythematoid type of basal cell epithelioma. One can usually recognize such growths clinically.

DR. WILBERT SACHS: I think that clinically only a tentative diagnosis can be suggested. Microscopic examination should be made. I believe that on clinical grounds alone it is not always possible to differentiate between a superficial basal cell epithelioma and Bowen's disease.

DR. ISADORE ROSEN: One should be able to make a differential diagnosis clinically between basal cell epithelioma and Bowen's disease. The former has features which are quite different from those of the latter. In this instance I believe the condition is a superficial form of basal cell epithelioma.

DR. ANTHONY C. CIPOLLARO: My clinical diagnosis of this lesion is superficial basal cell epithelioma. Lesions like the one presented tonight are often mistaken for Bowen's precancerous dermatitis.

DR. GEORGE M. LEWIS: In looking through the literature, I was struck with the difference in descriptions given for Bowen's disease. Cases with the clinical appearance of the lesion present in this patient have shown the histologic changes of Bowen's epithelioma. I agree that the most likely diagnosis is epithelioma of the flat type.

A Case for Diagnosis (Parapsoriasis?). Presented by DR. MAX SCHEER.

A. A., a man aged 52, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 13, 1940, with an eruption of the face, arms, and legs of one year's duration.

The patient presents ill defined, slightly yellowish patches scattered over the face, forehead, arms, legs and torso. Some of the lesions are slightly edematous. He complains of pruritus.

The Wassermann and Kahn tests gave negative reactions.

Histologic examination showed a "superficial dermatitis."

DISCUSSION

DR. DAVID BLOOM: I should like to know how long parapsoriasis may exist without showing microscopically the features of parapsoriasis. I have in mind a patient of mine with parapsoriasis en plaques of five years' duration in whose case Dr. Satenstein's histologic report was dermatitis.

DR. WILBERT SACHS: Much depends on what tissue is taken for biopsy. This patient has on the arms the clinical features of parapsoriasis. I believe that tissue from the body would not show the picture of parapsoriasis. A biopsy specimen in this case should be taken from the arm.

A Case for Diagnosis (Schamberg's Disease?). Presented by DR. MAX SCHEER.

M. R., a man aged 40, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 10, 1940, with an eruption on the outer part of the left ankle of two years' duration.

Two years ago a patch of brownish discoloration appeared above the left ankle. Eight months ago a similar patch appeared on the left shin, and three months ago another patch appeared above the outer aspect of the right ankle. There is a patch the size of a silver dollar above the left ankle which is brownish and has a pur-

puric dark center the size of a 25 cent piece. The whole patch is more or less lichenified. The patch on the left shin is brownish, and the one near the right ankle is large and elongated. There are no subjective symptoms. The lesions are of the same color, there is no fading on pressure. There is no history of her having taken drugs except acetylsalicylic acid frequently for headaches and colds. There are a few cayenne pepper red spots in some of the lesions.

A complete blood count showed the following: hemoglobin 88 per cent, erythrocytes 4,500,000, leukocytes 7,450 and platelets 210,000 per cubic millimeter, with a differential count of 64 per cent polymorphonuclear leukocytes, 28 per cent lymphocytes, 2 per cent eosinophils, 1 per cent basophils and 5 per cent monocytes. The tourniquet test gave negative results.

• DISCUSSION

DR WILBERT SACHS I saw some small cayenne pepper spots, and I thought I saw a few papular lesions. With papular lesions, one would have to also consider Gougerot's pigmented and purpuric lichenoid dermatitis.

DR ANTHONY C CIPOLIARO The diagnosis of Schamberg's progressive pigmentation is seldom made. From what I read about that disease, I think the condition in this case fits in with that diagnosis.

DR GEORGE M LEWIS One lesion halfway between the ankle and the knee is directly under the leather in his garter. I think that this particular lesion is due to sensitivity to leather or dye.

Lupus Erythematosus and Lichen Planus Presented by **DR MAURICE J COSTELLO**

S W, a Jewess aged 55, from Bellevue Hospital, presents two distinct eruptions. The lesions on the forehead and lower lip have been present for four years and for seventeen months, respectively, and those on the mucous membranes of the mouth for four and a half years. The lesion on the left side of the forehead near the hair line is round, erythematous and infiltrated and has an adherent scale. It is atrophic and telangiectatic. There is a similar half dime-sized lesion on the left side of the lower lip.

A biopsy specimen of tissue from the lesion on the forehead showed lupus erythematosus.

The lesions on the oral mucous membranes are typical of lichen planus, consisting of milky white dots, circles, strands and bands forming a reticulated network. A biopsy specimen of one of the lichen planus papules on the inner sides of the thigh, which has faded, showed lichen planus.

A complete blood count was normal. The Wassermann reaction of the blood was negative, and the blood sedimentation rate was 21 mm in one hour.

A Case for Diagnosis (Necrobiosis Lipoidica?) Presented by **DR MAURICE J COSTELLO**

M S, a Jewess aged 35, from Bellevue Hospital, had pertussis and lobar pneumonia five years ago. Her mother has diabetes. A roentgenogram of the chest showed no tuberculosis. A roentgenogram of the sinuses showed slight hypertrophic mucosal changes of the right maxillary sinus. Several examinations of the urine for sugar have given negative results. The eruption which she presents is confined to the anterior surface of the legs. There are about a half-dozen irregular, sharply demarcated, infiltrated, bluish red, shiny lesions which range in size from a few millimeters to a centimeter. On pressure there is a play of color but yellow predominates. The histologic examination of one of the lesions showed that the skin was infiltrated in scattered small areas by a great number of lymphocytes and plasma cells. There was an accompanying hyperplasia of the fibroblasts. The diagnosis was "chronic productive inflammation."

MINNESOTA DERMATOLOGICAL SOCIETY

CARL W. LAYMON, M.D., *President*F. W. LYNCH, M.D., *Secretary*

March 15, 1940

Erythema Induratum. Presented by DR. H. E. MICHELSON, Minneapolis.

Mrs. E. H., a white woman aged 52, has had nodules on the legs, arms and abdomen for several years. These lesions appear and disappear at irregular intervals.

She has sclerosing keratitis of the right eye, which is thought to be tuberculous. There are variously sized subcutaneous nodules from 0.5 to 4 cm. in diameter on the legs, thigh, abdomen and elbow region of the arm. The nodules are firm and are not ulcerated.

Erythema Induratum. Presented by DR. H. E. MICHELSON, Minneapolis.

L. L., a white woman aged 39, has had tender nodules on the legs (especially the calves) at intervals for over four years. She was first seen at the University of Minnesota in April 1939. The histologic observations were consistent with a diagnosis of erythema induratum. The Mantoux test, with a dilution of 1:1,000, gave a positive result. A roentgenogram of the chest showed obliteration of the left costophrenic angle, probably due to thickened pleura. There was no active pulmonary tuberculosis.

At present there is only a red, tender subcutaneous nodule 2 cm. in diameter on the right calf.

DISCUSSION ON CASES OF DR. MICHELSON

DR. F. T. BECKER, Duluth: I have observed an interesting clinical sequence in the past three years. I first saw a woman with classic erythema nodosum, and because of persistent fever and cough a roentgenogram of the chest was taken, which showed a minimal tuberculosis. She was placed in a sanatorium for one year and discharged one and one-half years ago. When I saw her the other day she had classic erythema induratum.

DR. HAMILTON MONTGOMERY, Rochester: I have seen tuberculous erythema nodosum (probably better designated nodose erythema induratum) persist for ten years or more without any of the lesions becoming ulcerated and yet in association with quiescent or active systemic tuberculosis elsewhere in the body. The section in the first case definitely showed the nodose type of tuberculosis with caseation, supporting a histologic diagnosis of erythema induratum.

DR. F. W. LYNCH, St. Paul: In a recent case of erythema nodosum the Mantoux reaction had been negative several months previously but became 3 plus during the course of the eruption. Microscopic study did not show any resemblance to erythema induratum, nor was there a tuberculoid reaction.

Juvenile Xanthoma. Presented by DR. JOHN F. MADDEN, St. Paul.

T. G., a boy aged 5 months, is presented. When he was 2 months old the mother noticed a millet seed-sized papule on the calf of the left leg. This increased steadily until it is now about the size of a lima bean. Since that time four more papules have appeared, one on the top of the head, one on the back, one on the extensor surface of the right arm and one on the calf of the right leg. These are distinctly yellow to orange, firm and painless and have increased slowly in size. The Wassermann reaction of the blood was negative. The urine was normal.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester: Even with stains for fat I could see no typical xanthoma cells. There were some endothelial giant cells, decided fibrosis

and increase in histiocytic cells, which would fit in with lesions of nevoxanthoendothelioma undergoing involution. This condition usually occurs as solitary papules or groups of lesions and undergoes spontaneous involution within a few months or years. The mother states that several of the lesions in this case are already disappearing. The other possible diagnosis would be multiple histiocytoma, in which case pronounced deposition of iron might be demonstrated. This condition should definitely be distinguished from juvenile xanthoma, in which the blood lipoids are usually elevated and in which there is often associated severe cardiovascular disease.

DR L. H. WINER, Minneapolis. I agree with the diagnosis made by Dr. Montgomery of nevoxanthoendothelioma, McDonough type. In the frozen section, stained for fat, I was unable to determine fat substance in the amount one would expect from the color of the lesions.

Multiple Hemangiomas Presented by DR H. E. MICHELSON, Minneapolis

D. A. L., a white girl aged 4 months, has had numerous birthmarks on her body. There has been no change since birth.

There are twelve strawberry hemangiomas at various points on the trunk and extremities varying from 1 to 3 cm. in diameter.

A Case for Diagnosis (Hemangioma?) (Purpuric Lichenoid Dermatitis?)

Presented by DR JOHN F. MADDEN, St. Paul

H. M. aged 21, is presented. The patient's mother noticed a light brown discoloration on the anterior surface of the junction of the middle and lower third of his left leg when he was 2 years of age. This lesion has gradually increased in size until it involves the anterior and medial surfaces of the lower half of the leg. The color has deepened and changes to violaceous in portions and dark brown in other portions. The patient has noted pain and discomfort during the past two or three years, since he has been working and standing on his feet most of the day.

The eruption is composed of irregular, rather superficial, scaling plaques associated with millet seed-sized to pea-sized maculopapules at the borders of the plaques. There are also varicose veins in the left leg.

DISCUSSION ON CASES OF DR MICHELSON AND DR MADDEN

DR HAMILTON MONTGOMERY, Rochester. There is no reason why the small hemangiomas of the baby could not be treated with radium, solid carbon dioxide or roentgen rays, although many dermatologists feel that some of these lesions may disappear spontaneously. If plastic surgery is to be considered, it is often well to wait until the child is of an age at which he is able to cooperate.

DR F. W. LYNCH, St. Paul. Lister, in a recent review of strawberry and cavernous angiomas (*Lancet* 1 1429, 1938), found that the majority disappeared entirely and almost all showed improvement without any treatment. Perhaps one should be less anxious to treat such lesions, particularly when their nature and location suggest that the result might not be particularly satisfactory.

DR STEPHAN EPSTEIN, Marshfield, Wis. One has to consider that the radio-sensitivity of hemangiomas usually is greater during the first year of life than afterward. Therefore, by postponing treatment the best time for radium treatment may be missed.

Mixed Cell Epithelioma Arising from Hair Follicle in a Boy Aged 11 Years Presented by DR JOHN F. MADDEN, St. Paul

R. D. S., a boy aged 11 years, was brought to the Ancker Hospital because of a lesion on the left side of the upper lip. His father said that the lesion had appeared as a firm, pinhead-sized papule during the summer of 1936, when the

patient was 7 years of age. The lesion enlarged slowly, and a crust appeared on its surface. The paternal grandfather died of carcinoma of the stomach with metastasis to the liver. There is no history of cancer or xeroderma pigmentosum in other members of the family. Now the papule is about the size of a large pea, firm and painless and has a superficial ulcerated center and a shiny, polished border.

DISCUSSION

DR. L. H. WINER, Minneapolis: My diagnosis on the basis of this microscopic section is a mixed basal-squamous cell carcinoma of hair follicle origin.

DR. HAMILTON MONTGOMERY, Rochester: Histologically, I thought this condition was an epithelioma adenoides cysticum and not a basal-squamous cell epithelioma. The cells were differentiated, and material with few mitotic figures and other features of epithelioma adenoides cysticum were present. Clinically, however, the lesion looked more like an ordinary basal cell epithelioma.

Pemphigus Erythematodes (Senear-Usher). Presented by DR. H. E. MICHELSON, Minneapolis.

Mrs. I. D., a white woman aged 34, noticed a small round scaly spot on the left side of the nose in the fall of 1936. This lesion often bled when she washed her face. The lesion did not change in appearance. In the spring of 1937 a similar but larger spot appeared on the scalp, and a short time later others developed on the chest and on the face. During the winter of 1937 to 1938 these areas almost completely disappeared, but they recurred again in the spring and were much more severe, especially in the region of the chest and the scalp. There is severe itching, especially during warm weather. On several occasions bullae were seen. The hair is rather oily. There are numerous variously sized lesions, with a thick firmly adherent scale on the scalp. Lateral to the nose and extending over the dorsum of the nose is a light red scaly indurated lesion showing dilated follicles. There are many lesions on the chest of different sizes. Those areas in which healing has occurred show a thin scar. There are similar lesions on the back.

Boeck's Sarcoid. Presented by DR. CARL W. LAYMON, Minneapolis.

J. L., a white woman aged 30, noted an eruption on her arms, shoulders and back in the spring of 1938. She had pulmonary tuberculosis at the age of 11 years, which soon healed, and she has remained entirely well since. Purpura and a severe cough developed after seven injections of gold sodium thiosulfate. After treatment with small injections of neoarsphenamine a moderately severe arsenical dermatitis appeared, making it necessary to discontinue administration of that drug. Other treatment consisted of intramuscular injections of bismuth subsalicylate, administration of arsenic trioxide (Asiatic pills) and vitamins and generalized ultraviolet irradiation.

The lesions are reddish brown, firm nodules, 0.3 to 1 cm. in diameter situated on the arms, face, shoulders and back. The Mantoux reaction, with a dilution of 1:1,000, and the Wassermann reaction were negative. A roentgenogram of the chest showed no evidence of tuberculosis or any other pulmonary changes.

Book Reviews

The Malarial Therapy of General Paralysis and Other Conditions By William H Kupper, M D, formerly resident physician of the Florida State Hospital and Special Physician associated with the Station for Malaria Research, International Health Division of the Rockefeller Foundation, Tallahassee, Fla Price, \$2.25 Pp 155, with illustrations Ann Arbor, Mich Edwards Brothers, Inc, 1939

This small volume is designed to give information to the interested reader on the use of malaria in the treatment of dementia paralytica and allied conditions. In part this demand is satisfied.

At the Florida Hospital the sexual type of malarial parasite is preferred. Consequently 8 pages are devoted to the cultivation of the anopheline mosquito. Such a procedure would hardly be used in most parts of the United States. Not only is it too complicated, but sexual transmission is longer drawn out and requires more hospital days. Altogether the procedure is more expensive. The method advised at the Florida Hospital is to allow spontaneous remission of the disease rather than the use of quinine—the quartan type of malaria is used there. This advice would hardly be tenable generally. Certainly if this procedure were the custom at clinics where the tertian strain is used, there would be grave danger of a high death rate. The author uses the oral temperature as the index of the fever. This is not a true interpretation of the temperature. Moreover, if the temperature is taken only once an hour during chills, peaks will be missed and poor indications of the patient's true condition will be given. The temperature should be taken at least every thirty minutes, or better every fifteen minutes during chills. It is realized that the author's work was done in a state hospital.

Not enough space in the book is devoted to the complications of malarial therapy—only about 4 pages. The writer does not think it is necessary to make chemical studies of the blood of his patients if they are followed closely clinically. This is highly questionable. His only reference to blood pressure is that the course of malaria should be stopped if the blood pressure falls to 90 mm of mercury systolic. Surely this subject should have been elaborated on.

The expert may get a few points of interest from the book. There is no doubt that the writer knows malaria. The book, however, is hardly calculated to be a guide to the physician preparing to take up the use of malaria therapy in the treatment of syphilis of the central nervous system. A long, although not complete, list of references is appended. The index also is extensive but not complete, e g, there is no index to blood pressure.

EFFECT OF THIOSULFATE ON ARSENIC EXCRETION

MARJORIE R. MATTICE, M.S.

HERMAN BAXT, M.D.

AND

JOHN M. BYRNE, A.B.

NEW YORK

It is our purpose not to cite the numerous opinions to be found in the literature regarding the effect of thiosulfate on urinary excretion of arsenic, since this has recently been ably reviewed by Muir, Stenhouse and Becker,¹ but to attack this controversial problem from an experimental angle.

Injections of thiosulfate are given for two purposes: (1) to relieve dermatologic symptoms and (2) to aid in diagnosis, the theory being that a course of thiosulfate will lead to exaggerated arsenic excretion in cases in which this element is stored in the tissues. In some clinics it has been the custom to administer thiosulfate on Monday, Wednesday and Friday in 1 Gm. doses and to instruct the patient to collect a twenty-four hour specimen of urine for examination as to arsenic content on the following Saturday. It was this practice which originally interested one of us (M. R. M.) in the question, since specimens thus collected frequently contained so little arsenic that the dermatologists registered complaints with the laboratory. In short, patients with apparent arsenical dermatitis failed repeatedly to respond to thiosulfate by excreting arsenic as measured in the twenty-four hour output of urine.

To determine the advisability or necessity of continuing this practice, patients were sought who would agree to be hospitalized and to follow instructions in an intelligent and cooperative manner. After a study of a small but well controlled group Mattice and Weisman² reported that

From Riker's Island Hospital and the Laboratory of Pathological Chemistry, Department of Medicine, New York Post-Graduate Medical School and Hospital.

1. Muir, K. B.; Stenhouse, E., and Becker, S. W.: Action of Sulfur-Containing Compounds in Arsenical and Mercurial Poisoning, *Arch. Dermat. & Syph.* 41:308 (Feb.) 1940.

2. Mattice, M. R., and Weisman, D.: Urinary Excretion of Arsenic: II. The Influence of Thiosulfate, *Am. J. M. Sc.* 193:420 (March) 1937.

intravenous injections of sodium thiosulfate do not increase the urinary elimination of arsenic but tend to diminish it, not only on the day of injection but subsequently. While these subjects were suspected of exposure to sufficient arsenic to cause their symptoms, actual proof thereof was lacking. More recently ³ further confirmation of the negative effect of thiosulfate has been obtained in a case of arsenical dermatitis under rigidly controlled circumstances.

With the belief, however, that more conclusive information could be secured by testing patients receiving arsenical treatments, search was made among the syphilitic persons in the penitentiary on Riker's Island for a suitable subject. Although control of diet is extremely important for subjects with an unknown arsenical history, it is of less consequence when arsenicals are introduced during the observation period. A survey of the prison diet revealed that its probable arsenic content was considerably less than average. Cereals constituted a much larger proportion of the diet than did fruits and vegetables of the sort which are commonly subjected to arsenical sprays. It was assumed, therefore, that the daily output from dietary sources ⁴ would not exceed 0.35 mg., results being expressed as arsenic trioxide. This assumption is supported by the data secured under control conditions.

EXPERIMENTS

Urine was collected over a five week period except on Sundays. This day was omitted since the patient could not be kept under the close scrutiny otherwise maintained. The findings are presented in table 1. When the arsenical and the thiosulfate were given an hour apart (fourth week) the suppression of urinary arsenic was almost incredible. Analyses were done in triplicate by the Osterberg electrolytic Gutzeit method ⁵ under conditions previously stipulated ⁶. That arsenic was not lost was evidenced by the remarkable output in the fifth week.

This was not the first time that such behavior had been observed. Earlier attempts to carry on studies through the clinic of the prison had been stopped when the sort of results shown in table 2 were encountered. Despite evidence to the contrary, it was felt that some "slip-up" had occurred. The subject reported in table 3 had reacted unfavorably to arsenical treatment and was undergoing a course of injections of thiosulfate prior to resumption of antisyphilitic measures. The record of the twenty-four hour volumes of urine was mislaid, so that the daily

3 Abiamowitz, E. W., and Mattice, M. R. Unpublished data, 1940.

4 Mattice, M. R., and Weisman, D. Urinary Excretion of Arsenic. I. Normal Subjects, *Am J M Sc* **193** 413 (March) 1937.

5 Osterberg, A. E. A Modification of the Electrolytic Gutzeit Apparatus for the Estimation of Arsenic in Biological Material, *J Biol Chem* **76** 19 (Jan) 1926.

6 Mattice, M. R. Chemical Procedures for Clinical Laboratories, Philadelphia, Lea & Febiger, 1936.

output of arsenic is not determinable. The concentrations, however, are significant. The third week was intended as a control period without medication. Because of the unexpected results, the investigation

TABLE 1.—*Urinary Output of Arsenic After Administration of Neoarsphenamine and/or Sodium Thiosulfate**

	First Week	Second Week	Third Week	Fourth Week	Fifth Week
Monday					
Medication	Neo- arsphen- amine	Sodium Thio- sulfate	Neo- arsphen- amine	Neo- arsphen- amine
Urine volume, in cubic centimeters.....	1,120	1,850	2,350	2,350
Arsenic, in milligrams of As ₂ O ₃ per hun- dred cubic centimeters.....	0.18	0.20	0.14	0.20
Total arsenic, in milligrams of As ₂ O ₃	2.01	3.70	3.29	4.70
Tuesday					
Medication	Neoarsphen- amine, sodium thiosulfate
Urine volume, in cubic centimeters.....	840	1,210	1,760	1,875	1,400
Arsenic, in milligrams of As ₂ O ₃ per hun- dred cubic centimeters.....	0.50	0.17	0.60	0.07	0.80
Total arsenic, in milligrams of As ₂ O ₃	4.20	2.06	10.56	1.31	11.20
Wednesday					
Urine volume, in cubic centimeters.....	1,120	1,400	1,750	1,820	1,960
Arsenic, in milligrams of As ₂ O ₃ per hun- dred cubic centimeters.....	0.50	0.14	0.40	0.06	0.50
Total arsenic, in milligrams of As ₂ O ₃	5.60	1.96	7.00	1.09	9.80
Thursday					
Urine volume, in cubic centimeters.....	1,120	1,850	1,680	1,790	1,175
Arsenic, in milligrams of As ₂ O ₃ per hun- dred cubic centimeters.....	0.25	0.06	0.40	0.05	0.70
Total arsenic, in milligrams of As ₂ O ₃	2.80	1.10	6.72	0.90	8.22
Friday					
Urine volume, in cubic centimeters.....	1,030	2,325	1,400	840	1,625
Arsenic, in milligrams of As ₂ O ₃ per hun- dred cubic centimeters.....	0.35	0.04	0.36	0.03	0.50
Total arsenic, in milligrams of As ₂ O ₃	3.60	0.93	5.04	0.25	8.12
Saturday					
Urine volume, in cubic centimeters.....	840	1,760	1,400	1,760	1,450
Arsenic, in milligrams of As ₂ O ₃ per hun- dred cubic centimeters.....	0.20	0.08	0.25	0.015	0.50
Total arsenic, in milligrams of As ₂ O ₃	1.68	1.41	3.50	0.26	7.25

* Read down the table for arsenic excretion (total per day shown in bold face numbers). Neoarsphenamine (0.6 Gm.) and sodium thiosulfate (1 Gm.) were given in the morning on alternate Mondays except for the fourth week, when the arsenical was administered on Tuesday at 9:30 a. m., followed by the thiosulfate exactly one hour later. The arsenic excreted the first week totaled 17.88 mg., but the amount is incomplete, since the first day's specimen was not obtained. The second week's total was 9.47 mg., without obvious effect from the thio-sulfate. The totals for the third and the fifth week were 39.81 mg. and 49.29 mg., respectively. As arsenic accumulates in the body and administration continues, there is apparent effort to remove proportionately larger amounts. This may be a consequence of the injections of thiosulfate, but the suppressing effect in the fourth week is very noticeable, only 3.81 mg. of arsenic being excreted in the five days following the injections (Monday's output is added to the previous week's total).

was terminated as unsatisfactory. In the light of later findings, it is unfortunate that the experiments were not completed.

Prepared ampules of sodium thiosulfate solution containing 1 Gm. of the drug were employed in these studies. Like Ayres and Anderson,⁷

7. Ayres, S., Jr., and Anderson, N. P.: Sodium Thiosulfate and the Elimination of Arsenic, J. A. M. A. **110**:886 (March 19) 1938.

we have never been convinced of the superiority of freshly dissolved sterile crystals. Although chemical deterioration (evidenced by precipitation of sulfur) is likely to occur in open containers, properly prepared ampules should not suffer in this regard.

TABLE 2—*Urinary Output of Arsenic After Administration of Mapharsen and Sodium Thiosulfate*

Date	Volume of Urine, in Cc	Urinary Excretion of Arsenic as As_2O_3		Medication
		Mg per 100 Cc	Total Mg	
5/ 9	1,000*	0.01	0.10*	0.06 Gm mapharsen, 1 Gm sodium thiosulfate one hour later
5/10	850	0.40	3.40	
5/11	900	0.16	1.44	
5/15	1,200	0.05	0.60	0.06 Gm mapharsen, 1 Gm sodium thiosulfate one hour later
5/16				
5/17	825	0.40	3.30	
5/18	1,700	0.08	1.36	
5/19	800	0.06	0.48	
5/22	1,350	Negative	Less than 0.10	None
5/23	1,400	0.01	0.14	
5/24	1,500	0.01	0.15	
5/25	1,300	0.03	0.39	
5/26	1,015	0.02	0.20	

* Record of twenty four hour volume missing, results expressed per liter

TABLE 3—*Urinary Excretion of Arsenic After Administration of Sodium Thiosulfate*

Date	Volume of Urine, in Cc	Urinary Excretion of Arsenic as As_2O_3		Medication
		Mg per 100 Cc	Total Mg	
5/ 3				1 Gm sodium thiosulfate
5/ 4	1,000*	0.01	0.10*	1 Gm sodium thiosulfate
5/ 6	1,000*	0.02	0.20*	
5/ 8	1,000*	Negative	Less than 0.05*	
5/ 9	1,000*	Barely detectable	Approximately 0.05*	
5/10	1,000*	0.02	0.20*	1 Gm sodium thiosulfate
5/11	600	0.01	0.05	
5/17				1 Gm sodium thiosulfate
5/22	1,175	0.008	0.09	None
5/23	1,180	0.005	0.06	
5/24	1,075	0.005	0.05	
5/25	800	0.01	0.08	
5/26	1,075	Negative	Less than 0.05	

* Record of twenty four hour volume missing, results expressed per liter

COMMENT

Although the beneficial effect of sodium thiosulfate in dermatologic practice is usually ascribed to augmented urinary excretion of arsenic, the findings of various investigators in this regard are contradictory.

Even Kuhn and Reese,⁸ who offered proof of increased arsenic excretion after the administration of sodium thiosulfate, admitted that the decided increase is of short duration and cannot be maintained by subsequent doses of the thiosulfate.

In part, differences in results may be due to the procedures employed. Many of the most ardent American advocates of the theory of arsenic mobilization under thiosulfate therapy have a common origin, which is reflected in their method of expressing the results of laboratory analyses, viz., in terms of metallic arsenic per hundred grams of dry specimen (C. N. Myers). Under these conditions, the arsenic will vary not alone in its concentration in the body fluid tested but also in changes in the solid content. In blood the variation in total solids and water is strictly limited, but in urine wide differences exist. It is conceivable that urinary arsenic when computed per hundred grams of solids may not present the same picture as when the data are given in terms of twenty-four hour output. The more conventional system of expressing laboratory findings employs milligrams per hundred cubic centimeters for blood and milligrams per day for urine, the results being given either as arsenic or as arsenic trioxide (the former amounting to 75.7 per cent of the latter).

The most recent contribution to the literature of the Myers group is that of Ayres and Anderson.⁷ They presented 49 cases of various dermatologic conditions in which arsenic was suspected of being a causative factor. In 8 per cent of these, there was failure to excrete arsenic before or after injection of sodium thiosulfate; in 12 per cent there was a decrease in the output of arsenic, and in 80 per cent an increase was demonstrated, which in some instances was very high (results expressed on the dry basis). Their subjects were not restricted or controlled in any way. They described the collection of specimens as follows:

The patient is given a sterile quart glass jar with a glass top (in order that no metal which might possibly contain arsenic may come in contact with the urine) and is instructed to fill the jar with portions of each urination over a twenty-four hour period. When this is brought back he is instructed to empty his bladder, is given 1 Gm. of sodium thiosulfate in 10 cc. of sterile distilled water intravenously and is then instructed to urinate directly into a second jar until it is filled rather than to use samples over a twenty-four hour period.⁷

Although the clinician may feel that this casual collection of specimens suits his purpose, it is scarcely a scientific approach to the problem, regardless of how many patients are involved.

Since it is difficult to secure subjects who can be adequately controlled and to arrange for the extensive laboratory work, our cases have

8. Kuhn, H. A., and Reese, H. H.: Sodium Thiosulfate in the Treatment of Metallic Intoxication, *J. A. M. A.* **85**:1804 (Dec. 5) 1925.

been reported for such enlightenment as they may furnish. On the remote possibility that arsenic long deposited in the tissues might resist removal under the auspices of thiosulfate, it was deemed advisable to provide the subject with definite amounts of arsenic. Rather than hastening the exit of this element from the body, sodium thiosulfate actually suppressed its elimination in the urine. These findings confirmed the observations of Mattice and Weisman,² only more dramatically, since the quantity of arsenic involved was much larger.

It is agreed that the most suitable subjects for study would be those with frank postarsphenamine dermatitis, but it would be necessary to follow the progress of the ailment with and without thiosulfate. Such subjects are not likely to be available except for casual rather than thorough testing. Unless thiosulfate only mobilizes arsenic which has been deposited in the skin in amounts sufficient to produce characteristic symptoms, augmented output should be demonstrable in the case of any subject who has stored this element anywhere in the body. The ubiquitous use of arsenical compounds in Western civilization argues against the possibility of an adult having no arsenic in his body. Actually, the chances of "contamination" of the subject are so great as to necessitate extreme precautions. Many investigators reporting the role of thiosulfate showed evident lack of thorough control of the multitudinous factors which could have some bearing on the findings. As a consequence, much of the literature is scientifically meaningless.

The clinical use of sodium thiosulfate is based on foundations which apparently cannot be accepted unequivocally. The comment of a recognized authority in an outstanding American institution reflects the uncertainty which, though largely inarticulate, is widespread throughout the ranks of dermatology. "We use sodium thiosulfate only in very early phases of arsenical dermatitis, that is, during the first two or three days, hoping that it does tend to increase the arsenical output."

SUMMARY

We have obtained no evidence that sodium thiosulfate injected intravenously mobilizes arsenic from body stores for urinary elimination. Therefore, the administration of sodium thiosulfate for clinching the diagnosis of arsenical dermatitis is not warranted.

When an arsenical and a thiosulfate are injected within an hour of each other, in the order stated, the urinary excretion of the arsenic is decidedly suppressed.

This problem was planned under the direction of Dr. Milton A. Bridges. The intern and nursing staff of Riker's Island Hospital gave assistance.

NATURE OF THE EXCITANT OF POISON IVY DERMATITIS

BEDFORD SHELMIRE, M.D.

DALLAS, TEXAS

During the past half-century numerous attempts have been made to isolate and identify the toxic principle of the various species of the three leaflet, white-fruited forms of the *Rhus* family, scientifically known as *Rhus radicans* (*Rhus toxicodendron*), *Rhus quercifolia*, *Rhus microcarpa*, *Rhus rydbergii* and *Rhus diversiloba*, etc., and commonly known as poison ivy or poison oak. Some botanists still contend that slight differences exist between these many forms, basing their contentions on whether the habit of growth of the plant is chiefly erect or climbing and on variances in the texture, pubescence and degree of lobing of the leaflets. Since all these variations can be observed in the same species under different climatic, soil and other field conditions, conservative taxonomists now agree that the numerous species of poison ivy are identical. I have patch tested ivy-sensitive persons with acetone-diluted oleoresins extracted from the many so-called species of ivy collected in different sections of the United States and have found the antigenic potencies of the various specimens to be identical.

The oleoresin of the poison ivy vine or shrub has usually been considered the dermatitis-producing portion of the plant. Pfaff,¹ in 1897, obtained by alcoholic extraction of the branches and leaves of the poison ivy vine a toxic, nonvolatile oil, which he termed toxicodendrol. Acree and Syme, in 1906, employing ether as a solvent, obtained a toxic material designated by them toxicodendrin and considered a complex glycoside. McNair, in 1916, obtained from the poison oak (poison ivy) of the Pacific coast a highly antigenic oil, which he called lobinol. Majima and his co-workers and Toyama from 1916 to 1922 worked with alcoholic extracts of the sap of the Japanese lacquer tree (*Rhus vernicifera*). The yellowish toxic oil which they isolated was designated "urushiol." In 1934 Hill, Mattacotti and Graham extracted poison ivy of the eastern United States. They also obtained a yellow, toxic oil, which they concluded was identical with urushiol.

Dr. J. H. Black gave many valuable suggestions.

From the Department of Dermatology, Baylor University School of Medicine.

1. For complete bibliography see: Hill, G. A.; Mattacotti, V., and Graham, W. D.: The Toxic Principle of Poison Ivy, *J. Am. Chem. Soc.* **56**:2736 (Dec.) 1934.

In attempted desensitization to poison ivy, 28 ivy-sensitive persons were given single large or toxic doses of ivy oleoresin by mouth. Symptoms of intolerance, in order of frequency, were pruritus ani et vulvae, flare-up of healed patch test sites, generalized toxic dermatitis medicamentosa with predilection for areas previously affected by ivy dermatitis, pompholyx-like eruptions of the hands and feet and mild gastric upsets. Examination of the vulvae of the female volunteers, all of whom complained of extreme pruritus vulvae, showed intense erythema of the urethral orifice and surrounding area. This finding indicated that the dermatitis-producing excitant of the poison ivy oleoresin was excreted in the urine. Attempts were then made to determine whether this excitant was an oil or some urine-soluble fraction of the oil.

Water, saline solution and urine extracts of ivy leaves were prepared by adding the separate extracting fluids to equal volumes of triturated dried ivy leaves. The mixtures were allowed to stand for twenty-four hours at room temperature and were then passed through ordinary filter paper to remove plant particles. Patch tests with these various extracts routinely gave negative or doubtful reactions in ivy-sensitive persons. It had been previously proved that ivy oil obtained from the roots during the dormant period of the plant was two to ten times as potent as a similar quantity of oil extracted from the leaves at various periods of plant growth. Patch tests with water extracts of roots grubbed during the winter and passed through one layer of filter paper evoked strongly positive (vesicular) reactions in the same persons. Several passages through filter paper rendered these extracts nonantigenic. This decided variation in potency between specimens of oil extracted from the roots and from the leaves is apparently due to the large amounts of waxes, gums and waste products found in the latter. These experiments indicated that the dermatitis-producing excitant when found in water, saline solution and urine extracts of the plant was chiefly in suspension, as it could be removed by passage through ordinary filter paper.

A water extract of roots was then passed through gauze to remove contaminating particles of the plant. Patch tests with portions of this extract produced violent reactions in ivy-sensitive persons. After passage through two layers of ordinary filter paper, which removes a high percentage of the antigenic agent, the extract was centrifuged at high speed for thirty minutes. Material collected from the upper, middle and lower portions of this centrifuged specimen evoked doubtful or mildly positive reactions of equal intensity in ivy-sensitive subjects. This further indicated that the greater part of the ivy excitant contained in water extracts was in suspension. That a small portion was in solution is also indicated by the mild but equal reactions which were evoked when various portions of the centrifuged specimen were used for the testing material.

A pint jar was filled with root bark, which contains most of the oil of the root. The bark was covered with water and allowed to stand for forty-eight hours. The water extract was then passed through filter paper, mixed with equal parts of ether and thoroughly agitated, and the water was removed by means of a separatory funnel. The ether extract was then evaporated to dryness in a glass evaporating dish. A fine film remained after complete evaporation of the ether. Distilled water (1 cc.) was added to the dish. The film did not dissolve, and after thorough agitation this water was not antigenic by patch test for ivy-sensitive persons. Negative reactions to patch tests did not preclude slight solubility of the substance forming the film. The water was then evaporated by heating, since I had previously demonstrated that pure ivy oleoresins, antigenic urines and their watery dialysates, corn oil dilutions and watery suspensions of ivy oil lose no demonstrable amount of their dermatitis-producing potency through boiling over flame for from five to thirty minutes. Acetone (1 cc.) was then added to the dish and immediately assumed a straw color, through dissolution of the film. This acetone material was highly antigenic for ivy-sensitive persons but not for controls. Highly antigenic unfiltered water extracts of roots were then dialyzed through extraction thimbles. Patch tests with concentrated ether extracts of these watery dialysates gave doubtful to mildly positive reactions in ivy-sensitive subjects. These experiments indicate that the dermatitis-producing fraction of ivy oleoresin either is only slightly soluble in water or is so bound up in the oil that it is not easily separated by this agent.

I ingested 2 cc. of the 1 to 10 dilution of the ivy leaf oleoresin in corn oil. The approximate potency of this oleoresin was previously determined by the quantitative patch testing of persons of known sensitivity. After ingestion of this known dose, my urine and feces were collected for three days and extracted with ether. By employing quantitative patch tests with these extracts in subjects of known sensitivity, it was estimated that in a three day period approximately 30 per cent of the ingested dose was excreted in the urine and the remainder was eliminated in the feces. When an equal amount (10 cc. of a 1 to 50 dilution) of the oleoresin was injected intramuscularly, the percentages of the excitant found in the urine and feces were approximately the same as after ingestion of the oil. Traces of the ivy excitant could readily be demonstrated in the untreated urine of subjects taking small oral doses of the ivy oleoresin in attempted preseasonal desensitization. Patch tests with concentrated ether extracts of the urine of these persons evoked violent reactions. The urine of 1 patient who ingested massive doses of poison ivy oleoresin contained so much of the ivy excitant that a drop of her urine placed on the skin

of ivy-sensitive subjects and allowed to dry caused typical vesicular reactions. Patch tests with concentrated ether extracts of this urine elicited extreme reactions. The results of repeated control tests on nonsensitive persons were routinely negative. The dermatitis-producing fraction of the ivy oleoresin therefore proved freely soluble in urine if previously separated from the oleoresin by passage through the body.

Being nonsensitive to ivy, I ingested an ounce (28 cc) of the 1 to 10 dilution of an ivy oleoresin extracted from roots dug during the winter. Patch tests with untreated urine collected as late as seventy-two hours after ingestion of this large dose and repeatedly passed through ordinary filter paper evoked positive reactions in ivy-sensitive persons. Ether extracts of the daily urine output showed, by means of patch tests, traces of the ivy excitant present in the specimen through the fifth day. Patch tests with similar extracts of urine collected after the fifth day routinely gave negative reactions. Antigenic urines stored in the ice box or at room temperature routinely lost their potency after one month to six weeks. These experiments further indicate that the ivy excitant is freely soluble in urine.

At intervals of from six to eighteen hours after ingestion of this large oral dose 75 cc of my blood was collected. After coagulation the blood serum was agitated with an equal volume of ether. The ether extract of the serum was partially evaporated, kept at freezing temperature for one hour and filtered to remove fats. Patch tests with this ether extract gave typical vesicular reactions in ivy-sensitive persons.

A portion of my urine specimen was centrifuged at high speed for thirty minutes. Patch tests with 1 drop each of the upper, middle and bottom layers of this centrifuged specimen gave equally severe reactions, proving that the antigenic material in the urine was in solution and not in suspension. This further indicated that the antigenic material was not an oil but some urine-soluble fraction contained in the oleoresin.

A portion (3 ounces [85 cc]) of my first twenty-four hour urine specimen was dialyzed through both cellophane and parchment sacks. Patch tests with the watery dialysates and their concentrated ether extracts gave positive reactions in ivy-sensitive persons. Control tests gave negative reactions. Since oils are not dialyzable, these results indicate the dermatitis-provoking excitant to be a dialyzable fraction of the oleoresin.

One cubic centimeter of the ivy oil was vigorously shaken in 8 ounces (227 cc) of water, and this watery suspension was similarly dialyzed. Patch tests with the untreated and concentrated ether extracts of these dialysates produced negative reactions in ivy-sensitive persons. The dermatitis-producing fraction of the oleoresin is so firmly bound in the oil that it is insoluble or only slightly soluble in water in this chemical

state. After separation of this fraction from the oil by passage through the human body it becomes soluble in water and urine, since highly antigenic urine can be rendered completely nonantigenic by repeated dialyzation through cellophane into water.

CONCLUSION

My experiments indicate that the dermatitis-producing principle of poison ivy is not an oil, as previously described, but a dialyzable fraction of the oleoresin soluble in water and urine.

1719 Pacific Avenue.

PATHOLOGY OF SCHISTOSOME DERMATITIS

STERLING BRACKETT, PH D

CHAPEL HILL, N C

Since Cort¹ showed that a dermatitis contracted from the water on bathing beaches in northern Michigan was caused by the penetration of certain larval trematodes (schistosome cercariae) into the skin, this disease, schistosome dermatitis, has attracted increasing attention, particularly in the lake regions of the North-Central part of the United States, where tourist trade has been affected. Schistosome dermatitis, commonly called "swimmer's itch" or "water rash," has been most extensively investigated in Wisconsin,² Michigan³ and Manitoba.⁴ Results and conclusions of these combined investigations which relate to this paper may be summarized briefly as follows:

1 All or most of the dermatoses directly ascribable to contact with water while bathing in the areas investigated are caused by the penetration of schistosome cercariae into the skin. No other cause for the cases of so-called "swimmer's itch" could be definitely shown. While five or more dermatitis-producing cercariae have been reported in this country,

From the Department of Zoology, University of Wisconsin, and the Wisconsin State Board of Health

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1 Cort, W W. Schistosome Dermatitis in the United States (Michigan), J A M A **90** 1027-1029 (March 31) 1928

2 (a) Edwards, A C, and Brackett, S. A "Swimmer's Itch" Schistosome Dermatitis, Wisconsin M J **37** 543-547 (July) 1938. (b) Brackett, S. Methods for Controlling Schistosome Dermatitis, J A M A **113** 117-121 (July 8) 1939, (c) Studies on Schistosome Dermatitis. V Prevalence in Wisconsin, Am J Hyg (Sect D) **31** 49 (May) 1940

3 (a) Cort, W W. Studies on Schistosome Dermatitis. I Present Status of the Subject, Am J Hyg **23** 349-371 (March) 1936. (b) Talbot, S B. Studies on Schistosome Dermatitis. II Morphology and Life History Studies on Three Dermatitis-Producing Schistosome Cercariae, C Elvae Miller, 1923, C Stagnicola, n sp and C Physellae n sp, *ibid* **23** 372-384 (March) 1936. (c) Cort, W W, McMullen, D B, Olivier, L, and Brackett, S. Studies on Schistosome Dermatitis. VII Seasonal Incidence of Cercaria Stagnicola Talbot, 1936, in Relation to the Life Cycle of Its Snail Host, Stagnicola Emarginata Angulata (Sowerby), *ibid*, to be published

4 (a) McLeod, J A. Studies on Cercarial Dermatitis and the Trematode Family Schistosomatidae in Manitoba, Canad J Research (Sect D) **18** 1-28 (Jan) 1940. (b) Swales, W E. Schistosome Dermatitis in Canada. Notes on Two Causative Agents and Their Snail Hosts in Manitoba, *ibid* **14** 6-10 (Jan) 1936

three, namely, *Cercaria stagnicola*, *Cercaria elvae* and *Cercaria physellae*, account for most of the outbreaks.

2. The causative organisms as well as the disease are widespread in the lake regions of the North-Central states and neighboring Canadian provinces. Not every lake in these areas is troubled, since the cercariae must develop in certain snails before emerging into the water, and the snail hosts are not uniformly distributed. Suitable snail hosts are absent from many lakes.

3. Outbreaks of the disease occur most commonly in July and August, although they are occasionally encountered earlier or later in the summer.

4. Not all persons are susceptible. Children may be more commonly affected, probably because their activities in shallower water bring them in contact with more cercariae, and in addition they may be more sensitive than adults.

5. The clinical picture is about as follows: A few minutes after emerging from infected waters a tingling sensation is felt in the exposed parts of the body. Soon pinpoint-sized red macules may be observed. The tingling may then subside, and nothing is experienced for a number of hours, when a distinct itching arises and the macules enlarge to form firm, discrete papules from 2 to 5 mm. in diameter, which are red at first and may be surrounded by a halo of hyperemia. Occasionally the lesions become pustular. Secondary infections may cause certain variations. In very susceptible persons or in persons with severe infections after the cercariae invade. The lesions usually fade within a week, although a red or brown stain may persist longer. No difference was noted in the lesions caused by the different species of cercariae. The extremities are most frequently involved, and the face and neck are usually spared. The disease may be differentiated from dermatoses caused by other parasites.^{2a}

6. No evidence has appeared that these schistosomes are able to set up a systemic infection in human beings. In fact, all evidence is to the contrary. Cort suggested that the dermatitis seen in human beings is the manifestation of a defense mechanism against an organism that has accidentally penetrated into the wrong host species.

7. Where the disease occurs extensively it may be feasible to eliminate the snail hosts, which can be killed with certain copper compounds. If this is not practicable, the severity of attacks may be greatly reduced if individual bathers rub exposed parts of the body vigorously with a towel immediately on leaving infected water. Apparently the cercariae do not penetrate extensively until the water begins to evaporate on the surface of the skin. Rubbing with the towel crushes them before they have had a chance to enter.

The only information in the literature concerning the activity of the cercariae after they invade the skin and the response of the tissues to the organisms is in a report of some investigations in Europe by Vogel.⁵ He experimentally infected himself and volunteers with *Cercaria ocellata*, a European cercaria closely related to the schistosome cercariae of this country and possessing essentially the same dermatitis-producing properties. Twenty-four hours later he removed some of the tissue for histologic studies. Eleven cercarial bodies were found in this tissue, which was sectioned serially. These were lying in tunnels in the epithelial layer and were still easily recognized. Since Vogel's study did not demonstrate the final fate of the cercariae in human skin, several biopsies were made during the course of the Wisconsin investigations, with the hope of determining this matter. The results of the histologic studies of the serially sectioned material are discussed in this paper.

METHOD

The inner surface of the forearm was chosen as the site for the experimental lesions and for the removal of specimens for biopsy. The first set of lesions was produced with *C. elvae*, and the biopsy was made about fifty hours after exposure. An elliptic piece of tissue about 2.5 cm long and 1 cm wide was removed. A second set of lesions, produced by *C. stagnicola*, was excised about twenty-nine hours after the cercariae had entered. This piece of tissue was about twice the size of the first. It was taken from an area within a few centimeters from where the other specimen was removed. Both pieces of tissue were fixed in diluted solution of formaldehyde U. S. P. (5 per cent) immediately after removal. The tissues were sectioned serially about 6 microns in thickness and stained with hematoxylin and eosin. All sections of both sets of material were first inspected with lower powers of the microscope in order to determine the distribution of the cercariae and lesions. After this, many of the more important sections were studied carefully with higher powers of the microscope for histologic details.

HISTOLOGIC PICTURE

Twenty-Nine Hour Sections—Numerous burrows in the epithelium and evidence of an acute inflammatory reaction characterized the tissues twenty-nine hours after the invasion of the cercariae, although it was not possible to find any evidence of the cercarial bodies themselves. These burrows were traced from section to section and in several cases from a point where they entered on the surface to a place where they ended blindly, still within the malpighian layer. No evidence was seen which indicated that the cercariae had gone beyond this layer into the deeper tissues. For the most part the lesions were almost completely filled with neutrophils, which in places formed intraepithelial abscesses (fig. 1A). Generalized edema in the vicinity of the burrows and in the cutis and the

⁵ Vogel, H. Hautveränderungen durch *Cercaria ocellata*, Dermat. Wehnschr. 90: 577-581 (April 26) 1930.

subcutaneous tissue below them was pronounced. Lymph vessels were dilated and easily seen (fig. 1 *B*). The edematous condition was extensive in several places above the burrows, so that a considerable amount of fluid was concentrated just under the cornified layer to form the vesicles that were seen grossly. It seemed to be characteristic of the burrows that their walls were definite and sharp in outline. For the most part the epithelial cells surrounding them did not seem to be particularly changed.

It is interesting to compare the appearance of these twenty-nine hour sections with Vogel's observations on twenty-four hour sections. The most striking difference is that distinct cercarial bodies were seen by Vogel, while none were present in my sections. There seemed to be



Fig. 1.—Twenty-nine hour sections ($\times 123$). *A*, an extensive infiltration of neutrophils in the cercarial burrow and overlying lesion to form an intraepithelial abscess. *B*, a dilated lymph vessel in the cutis.

no significant difference in the depth of the penetration in either set of tissues. Vogel described some changes in the epithelial cells surrounding the canals, such as a dissolution of the intercellular material and consequent loosening of the tissues, vacuolation of the cytoplasm and pyknosis of the nuclei. His photographs indicate, however, that these changes were not extensive. He noted some collection of fluids and evidence of invasion of neutrophils and lymphocytes into and around the canals. This infiltration in Vogel's sections seems not to be as intense as that in mine. There was moderate edema in the cutis of the tissue studied by Vogel but no pronounced cell infiltration. Vogel interpreted the changes in the tissue as being due chiefly to the histolytic action of the secretions of the penetration glands of the cercariae (fig. 2).

Fifty Hour Sections—Again burrows were easily found in sections of lesions at this stage, but extensive search failed to reveal any cercarial bodies. The burrows were still confined to the epithelial layer, and in following some of them from section to section there was seen no evidence that the cercariae had penetrated into the deeper tissues (fig 3, A, B and C). The channels were filled in places with loosely arranged debris and with some recognizable neutrophils and lymphocytes. In

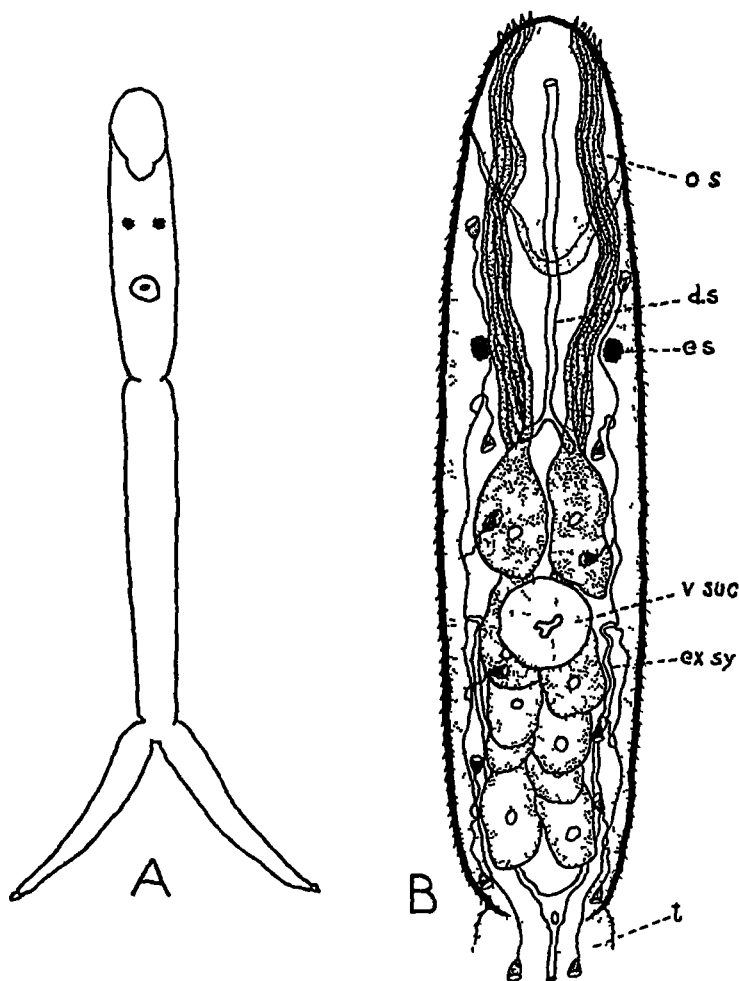


Fig 2—A, outline diagram of *C. elvae*, showing the relation of the body to the characteristically forked tail, which is lost before the cercaria penetrates into the skin of a host. B, diagrammatic drawing of body of *C. elvae*, showing the five pairs of large unicellular penetration glands. *os*, the oral sucker, *ds*, digestive system, *es*, pigmented eye spots, *v suc*, ventral sucker, *ex sy*, excretory system, and *t* the base of the tail.

other places the burrows were completely empty or showed evidence of having contained a more or less clear fluid. Above some of the burrows were edematous infiltrations between the malpighian layer and the cornified tissue. The acute inflammatory reaction seemed to have subsided considerably, but, in contrast to the picture in the earlier

sections, a striking invasion of eosinophils had occurred. The latter cells were present in large numbers in the subcutaneous and dermal tissues and formed a large percentage of the cells that could be identified within the lumens of the burrows and in the superficial edematous patches. Many of the tunnels at this stage were characterized by their

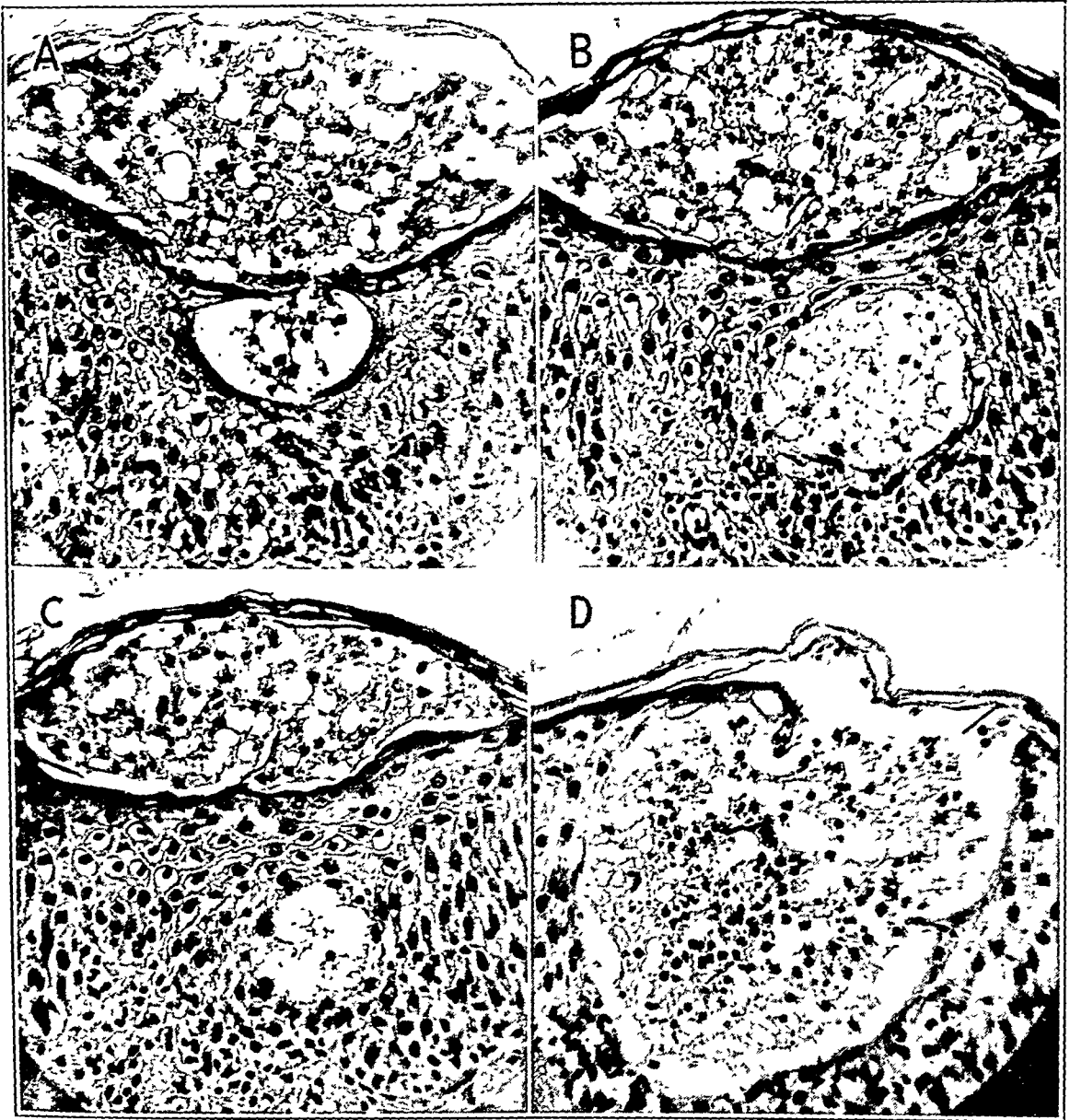


Fig. 3.—Fifty hour sections ($\times 123$). *A*, *B* and *C*, successive stages showing the horizontal movement of a cercaria in the epithelium. The beginning of the burrow where the cercaria has just entered the malpighian layer is seen in *A*. *B* shows a cross section of the burrow at about the center of its length, and *C* shows its termination. *D*, a large burrow. Eosinophils form a large part of the cellular contents of this lesion.

large diameters, some being four or more times the diameter of a cercaria (fig. 3 *D*). The large size of these tunnels may have been due to the histolytic action of the penetration glands of the cercaria.

COMMENT

Some of the differences between Vogel's material and mine have already been pointed out. It seems worth while to consider these in greater detail in an attempt to explain or correlate them if possible. At first the differences seemed almost qualitative, since Vogel found cercariae and I did not. On further analysis, the differences may be shown to be quantitative instead. I am convinced that cercariae were absent from my material not because they had gone on into deeper tissues where they could have been overlooked but because they had been destroyed, even as soon as twenty-nine hours after they had entered. If this assumption is correct, then it is only necessary to show that some persons respond more rapidly to the invasion of dermatitis-producing schistosome cercariae than do others, in order to explain the differences in the observations of Vogel and of myself. It has already been pointed out that there seemed to be evidence of a much more acute inflammatory reaction and of more extensive neutrophil invasion in my twenty-nine hour section than in Vogel's twenty-four section. This is hardly surprising, in view of the general evidence of individual variations which occur in other reactions. Specifically I have seen that the clinical manifestations of schistosome dermatitis may vary somewhat in different persons.

At this point it is significant to point out that I have been exposed to schistosome cercariae both experimentally and naturally many times each summer since about 1934 and that each year my reaction has been increasingly pronounced. At the outset the lesions were mild and caused little trouble, but by the time the biopsies were made in 1938 and 1939, penetrating cercariae would cause an almost immediate urticarial response. Within half an hour the area of penetration would be swollen, and often within twelve hours inflamed lymph vessels could be traced for more than half the length of the forearm. While Vogel did not give any evidence in his paper which would indicate the previous history of the person from whom he obtained his material, it is probable, judging from his descriptions, that it was someone who had had little or no previous contact with the organisms and who was apparently not unusually sensitive to them. From this evidence, then, it may be safe to conclude that the differences seen in the two sets of material are due to the different rates in which the tissues of the two subjects responded to the invasion of the cercariae. It seems that these two reports are good evidence that the cercariae are destroyed in the epithelial layers of the skin and that different persons react at different rates. Also, it is suggested that the speed of response may be increased in a person who has had previous contact with the specific organisms.

Assuming that the cercariae had not been destroyed in Vogel's twenty-four hour sections simply because the defense mechanism, in an apparently less responsive host, had not come into action as rapidly as in my experiments and that they would have been destroyed eventually, the following conclusions may be drawn concerning the course of schistosome dermatitis.

The cercariae penetrate into the epithelial layer of the skin but no deeper, although they may progress for a while horizontally in this layer. An acute inflammatory reaction results, and the cercariae are destroyed. Edema occurs at this time, which produces the lesions that are observed clinically. Following the neutrophil and lymphocyte invasion and destruction of the cercariae, there is an extensive invasion of all the surrounding tissues by eosinophils. It is assumed from clinical observations that the course from then on is one of recovery.

Some of the aforementioned evidence suggests that the immunologic phenomena associated with schistosome dermatitis might be well worth investigating. Only a few reports in the literature have a direct bearing on this question, and they are scanty. Culbertson⁶ described an antagonistic action of the normal serums of vertebrates against cercariae. He showed that against *C. stagnicolae* human serum showed a titer of 1:24, rat serum showed a titer of 1:48, and duck serum had no effect. The normal definitive host of this cercaria is not yet known, but other evidence suggests that it is likely some bird, a fact which fits readily enough with this observation of Culbertson's. Unfortunately, Culbertson did not discuss the source of his human serum; so the reaction of the person toward actual invasion by the schistosome cercariae is not known, but one can only conclude that the serum used did have a destructive action on the cercariae. Cort^{3a} reported a suggestive but brief experiment. Cutaneous tests with antigen obtained from the cercariae of *Schistosoma mansoni* were tried on about 20 persons in his laboratory in Baltimore. Of the whole group he alone gave a positive reaction. Since he was the only one who had a history of schistosome dermatitis, the positive reaction was attributed to previous exposure to the dermatitis-producing schistosome cercariae. These two reports combined with clinical observations and the histologic evidence given in this paper indicate that human beings possess naturally a mechanism that results in the destruction of these dermatitis-producing schistosome cercariae which accidentally penetrate into the skin and that previous contact may render the mechanism more rapidly responsive.

At present it is not possible to explain the so-called "immune" condition in certain persons who do not show a reaction after contact with

6. Culbertson, J. T.: The Cercaricidal Action of Normal Serums, *J. Parasitol.* 22:111-125 (April) 1936.

these cercariae. Either the cercariae find it impossible or unattractive to enter the skin or they may elicit no response at all while in the tissues of some persons. In view of the information contained in this paper, the latter proposition seems unlikely, however.

Further work along this line will undoubtedly enlighten the question of the nature and activity of the defense mechanisms in schistosome dermatitis.

SUMMARY

Sectioned biopsy specimens from lesions of patients with schistosome dermatitis were studied, and the histologic picture is described. The dermatitis-producing schistosome cercariae apparently were destroyed in the epithelial layer of the skin and did not reach the deeper tissues. There was an acute inflammatory response to the presence of the cercariae, with pronounced edema and extensive early infiltration of neutrophils and lymphocytes. Later, extensive invasion of eosinophils occurred. Clinical evidence suggested that recovery then follows rapidly.

Members of the surgery and pathology departments of the Wisconsin General Hospital assisted in preparing the material for study. Dr. E. A. Birge, Jr., and Dr. Nellie Bilstad gave helpful suggestions concerning interpretations.

XANTHOMA TUBEROSUM AND MYXEDEMA

REPORT OF A CASE

S. E. SWEITZER, M.D.

AND

L. H. WINER, M.D.

MINNEAPOLIS

As early as 1918 Luden¹ reported high cholesterol values, over 200 mg. per hundred cubic centimeters, in the blood of patients with myxedema. Mason, Hunt and Hurxthal,² studying the cholesterol content of the blood in patients with hyperthyroidism and hypothyroidism, observed that in hyperthyroidism there was no relation between the basal metabolic rate and the cholesterol content of the blood. However, they admitted that hyperthyroidism tends to diminish the blood cholesterol. In hypothyroidism they found an increase in the cholesterol content of the blood proportional to the decreased metabolic rate. They stated that true myxedema is accompanied by a high cholesterol content of the blood and that the cholesterol value is the important guide in the treating of patients with hypothyroidism. Low basal metabolic rates, without clinical evidence of myxedema, they noted, were accompanied by normal cholesterol values.

Rowland,³ in listing the lipid constituents of the blood, included three groups of compounds:

(1) The phosphatides: nitrogen and phosphorus compounds, such as lecithin and cephalin. The normal content of lecithin is 250 to 300 mg. per hundred cubic centimeters of blood.

(2) The cerebrosides: nitrogen compounds free of phosphorus.

From the Department of Dermatology and Syphilology, University of Minnesota Medical School, Dr. H. E. Michelson, Director, and the Department of Dermatology and Syphilology, Minneapolis General Hospital, Dr. S. E. Sweitzer, Chief.

1. Luden, G.: Studies on Cholesterol: V. The Blood Cholesterol in Malignant Disease and the Effect of Radium on Blood Cholesterol, in *Collected Papers of the Mayo Clinic*, Philadelphia, W. B. Saunders Company, 1918, vol. 10, pp. 470-485.

2. Mason, R. L.; Hunt, H. M., and Hurxthal, L. M.: Blood Cholesterol Value in Hyperthyroidism and Hypothyroidism: Their Significance, *New England J. Med.* **203**:1273-1278 (Dec. 25) 1930.

3. Rowland, R. S.: Anomalies of Lipid Metabolism, in Christian, H. A., and Mackenzie, J.: *Oxford Medicine*, New York, Oxford University Press, 1921, vol. 4, pt. 1, p. 214.

(3) The sterols nitrogen-free, phosphorus-containing compounds, such as cholesterol, fatty acids and their combination to form esters, also neutral fats and soaps. The normal cholesterol content of the blood is 120 to 180 mg per hundred cubic centimeters of blood.

Montgomery and Osterberg⁴ listed the lipids normally found in the plasma as follows. Total cholesterol amounted to 160 to 200 mg per hundred cubic centimeters, of which the cholesterol esters constituted about 70 per cent. The normal value for lecithin was 200 to 250 mg and the fatty acids totaled 335 to 350 mg per hundred cubic centimeters of plasma. The total lipid content averaged from 500 to 550 mg per hundred cubic centimeters of plasma.

Thannhauser and Magendantz⁵ classified xanthomas and reported on a physiologic study of 22 cases. They divided xanthomatosis into three main groups: (1) primary essential xanthomatosis, including the primary hypercholesteremic types, normal cholesteremic types and a combination of the hypercholesteremic and normal types, (2) secondary xanthomatosis due to lipemia and (3) localized xanthoma cell formation in true tumors. They discussed the physiology of hepatic disease associated with xanthomatosis, diabetes mellitus and xanthomatosis and the resultant diabetes insipidus following involvement of the pituitary and tuber cinereum by an infiltrate of xanthoma. They concluded that essential xanthomatosis is a cellular disease of the reticulum cells, caused by an intracellular disorder of their cholesterol metabolism.

Schaaf⁶ has shown that for the production of xanthoma the disturbance of lipoids in the blood need not be a permanent one. It could have been present during the formation of the xanthoma, after which the normal condition of the blood was restored.

Montgomery,⁷ presenting a working classification of cutaneous xanthomas, listed ten groups and the characteristics of each, both clinically and microscopically. He included in one of these groups xanthoma due to hepatic disease, which was characterized by lesions predominantly on the palms. He also listed xanthomas associated with cardiovascular disease, diabetes mellitus and the involvement of the pituitary region by xanthomatous deposits, with the resultant diabetes insipidus.

4 Montgomery, H, and Osterberg, A E. Xanthomatosis. Correlation of Clinical Histopathologic and Chemical Studies of Cutaneous Xanthoma, *Arch Dermat & Syph* **37** 373-402 (March) 1938.

5 Thannhauser, S J, and Magendantz, H. The Different Clinical Groups of Xanthomatous Diseases. A Clinical Physiological Study of Twenty-Two Cases, *Ann Int Med* **11** 1662-1746 (March) 1938.

6 Schaaf, F. On the Experimental Production of Xanthomas in Laboratory Animals, *J Invest Dermat* **1** 11-30 (Feb) 1938.

7 Montgomery, H. Cutaneous Xanthomatosis, *Ann Int Med* **13** 671-676 (Oct) 1939.

Neither Thannhauser and Magendantz nor Montgomery mentioned the association of myxedema with xanthomatosis. Fahr⁸ stated that he was unable to cite from his own experience or to find in the literature the association of xanthomatosis with myxedema.

REPORT OF CASE

History.—Mrs. K. L., a 44 year old white housewife, was first seen Dec. 7, complaining of melancholia, hoarseness and yellow discoloration of certain of her skin. In July 1936 she first noticed a reddish discoloration of the especially the left. In December 1938 she noticed that yellow transverse ridges began to form along the natural folds of the fingers and palms. Later the feet became involved in the same manner. At that time her menstrual periods became irregular and she became more melancholic. She also noticed that the skin of the entire body had become dry and scaly, and yellowish tumors appeared on the skin of the knees and feet.

Physical Examination.—Examination in December 1939 showed an apathetic, fairly well nourished woman. Her voice was hoarse, her hair dry and coarse and the skin of her entire body dry and scaly. The blood pressure was 120 systolic and 80 diastolic, and there was a soft systolic murmur at the apex of the heart. The pulse rate was 64. The skin was especially dry and scaly on the dorsal surface of the hands and forearms. Both palms were diffusely yellow, and there was an intensification of this color in the cutaneous creases, with the formation of variously sized nodules from 1 to 4 mm. in diameter. These nodules were within the epidermis and were not fixed to the underlying structures. There were also nodules on the knees (one on each, at the inferior border of the patella, 1.5 cm. in diameter). Other nodules from 3 to 6 mm. in size were arranged in groups on each achilles tendon. Tumors were also present at the base of the dorsum of the left great toe and at the base of the plantar surface of the right great toe. There was a narrow yellow band of infiltration 1 cm. long and 1 mm. wide on the lower conjunctiva of the right eye. The mucous membrane of the mouth was diffusely yellow. The tongue was enlarged and thickened. The remainder of the physical examination showed no abnormalities except for a dilated heart and electrocardiographic changes consistent with those found in myxedema. Examination of the vocal cords showed imperfect approximation due to partial loss of activity of the interarytenoid muscle, which was otherwise normal.

Laboratory Tests.—Roentgen examination of the skull and sella turcica showed no abnormalities.

The urine was yellow, slightly cloudy and alkaline and showed a faint trace of albumin. Its specific gravity was 1.009, and the microscopic study showed 1 to 4 pus cells and an occasional red blood cell per high power field.

The hemoglobin content of the blood was 50 per cent. The red cells numbered 2,530,000 and the white cells 5,200 per cubic millimeter. The differential blood count showed 55 per cent polymorphonuclear cells, 40 per cent lymphocytes, 2 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. The average mean diameter of the red blood cells was about 8.1 microns. The red blood cells showed moderate anisocytosis and slight polychromasia and poikilocytosis. The white blood cells appeared somewhat toxic, and the polymorphonuclear leuko-

8. Fahr, G. E.: Personal communication to the authors.

cytes showed toxic granulations and a few band forms. The blood picture suggested secondary anemia.

The basal metabolic rate was —28 per cent.

The chemical examination of the blood showed the icterus index to be 15 and the value for cholesterol 540 mg per hundred cubic centimeters. The tests for serum protein showed globulin 2.6 Gm and albumin 5 Gm per hundred cubic centimeters, making a total of 7.6 Gm per hundred cubic centimeters. The sugar tolerance test showed 85 mg of sugar per hundred cubic centimeters of blood during fasting, at one-half hour after ingestion of sugar, 115 mg, at one hour, 155 mg, at one and one-half hours, 140 mg, at two hours, 112 mg, and at three hours, 120 mg. The cholesterol tolerance test showed before the test, 565 mg per hundred cubic centimeters of blood, two hours after the ingestion of chole-



Fig 1—Patient with xanthoma tuberosum and myxedema, showing nodular lesions in the flexor folds of the hands

sterol, 800 mg, at four hours, 571 mg, at eight hours, 835 mg, and at twenty-four hours, 835 mg.

The urine after the lactose tolerance test was normal and showed no galactose, at two hours there was a trace, and at three, four and five hours it showed no galactose. The ascorbic acid content of the blood was 2 mg per hundred cubic centimeters.

Biopsies were made of three different areas of skin: skin from a tumor on the right toe and from one on the right knee and normal skin from behind the angle of the right mandible. Frozen sections were made and stained for fat with sudan III and Nile blue. The sudan III in the sections from the tumor showed red globular deposits, which extended the entire distance from the epidermis down to the lower part of the cutis. Sections stained with Nile blue showed only the neutral fats of the subcutis. Sections stained with hematoxylin and eosin showed areas of foam cells and Teuton giant cells adjacent to masses of mucinous degeneration, which lay between the connective tissue cells of the cutis.

Similarly stained sections of normal skin from behind the right mandible showed neither myxomatous degeneration nor xanthomatous deposits.

The microscopic diagnosis was xanthomatosis with myxedema.

Course.—The patient was given 3 grains (0.2 Gm.) of desiccated thyroid by mouth for one month, and on discharge from the hospital the dose was reduced to $1\frac{1}{2}$ grains (0.1 Gm.) per day. Examination on April 29, 1940 showed that the patient had improved, in that the skin was soft, the hair was oily, the hoarseness was gone, the tongue was smaller and she was cheerful and mentally alert. Her basal metabolic rate was +3 per cent, and the amount of cholesterol in the blood,

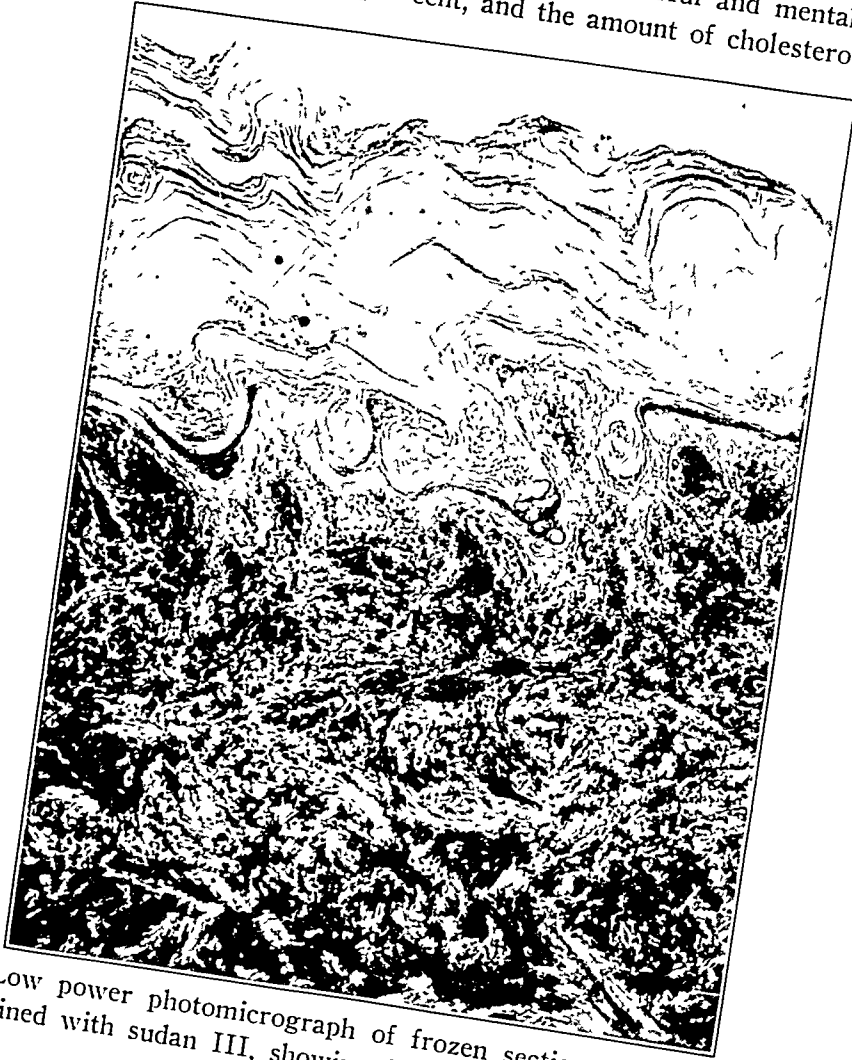


Fig. 2.—Low power photomicrograph of frozen section from a nodule of the great toe, stained with sudan III, showing fat deposits in the entire cutis. 260 mg. per hundred cubic centimeters. The tumors of the skin, although still present, were slightly smaller.

COMMENT

The patient filled all the requirements for a diagnosis of both myxedema and xanthoma tuberosum.

The diagnosis of myxedema was based on the clinical observations of melancholia, increased size of the tongue, hoarseness, dry skin and hair and the laboratory observation of lowered basal metabolic rate, increased cholesterol content of the blood, positive result of a cholesterol

tolerance test and the presence of myxedematous degeneration in the intercellular spaces of the cutis. The blood plasma had a lactescence due to the great increase of the cholesterol.

The diagnosis of xanthoma tuberosum was based on the clinical observations of yellow nodules present on the palms, knees, achilles tendon and plantar surfaces of both great toes. The histologic observation of foam cells containing globules which stained red with sudan III was conclusive evidence of xanthomatosis.



Fig 3—Low power photomicrograph of section from a lesion on the leg, stained with hematoxylin and eosin, showing myxomatous degeneration of the connective tissue.

No clinical or laboratory observations were suggestive of hepatic damage or diabetes mellitus. The facilities of our laboratory were not sufficient to make an analysis of all of the blood lipids.

SUMMARY AND CONCLUSIONS

We report a case of xanthomatosis and myxedema. The cholesterol content of the blood when we first saw the patient was 540 mg per

hundred cubic centimeters; it went to 835 mg. during the cholesterol tolerance test and at present is 260 mg. When the patient was first seen, her basal metabolic rate was —28 per cent; but after four months' therapy with desiccated thyroid, it was +3 per cent. Although the clinical picture of myxedema has disappeared, that of the xanthoma tuberosum remains.

In this case, a combination of xanthomatosis and myxedema is reported, both conditions being demonstrated clinically and histologically. We have been unable to find a similar occurrence in the literature.

We believe that the myxedema occurred first, together with hypercholesteremia, and that after trauma the cholesterol of the blood were deposited in the skin.

FUNGISTATIC POWER OF BLOOD SERUM

SAMUEL M PECK, M D

HERBERT ROSENFELD, M D

AND

ARTHUR W GLICK, M D

NEW YORK

If living fungi can be disseminated hematogenously from a primary focus to other areas of the skin, they can give rise either to new areas of mycotic infections or to dermatophytids. It has been suggested that these secondary lesions would be more common were it not for the fact that contact of the fungi with the circulating blood reduces their virulence¹ and even causes their destruction².

Per and Braude,³ as well as Jessner and Hoffman,¹ have apparently demonstrated fungicidal antibodies in patients with fungous infections. Furthermore, Ayres and Anderson² maintained that only patients with trichophytids have such humoral fungicidal substances. Based on such a premise, Traub and Tolmach⁴ used "convalescent serum" from patients with dermatophytids in the treatment of fungous infections. Lewis and Hopper⁵ were unable to substantiate the findings of Ayres and Anderson.²

These rather isolated but more or less related observations are of great importance in the conception of the whole problem of immunity.

Read at the Third International Congress of Microbiology, New York, Sept 6, 1939

From the Laboratories and Service of Dr Isadore Rosen, Mount Sinai Hospital, and from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital

1 Jessner, M, and Hoffman, H. Der Einfluss des Serums Allergischer auf Trichophytonpilze, *Arch f Dermat u Syph* **145** 187, 1923

2 Ayres, S, Jr, and Anderson, N P. Inhibition of Fungi in Cultures by Blood Serum from Patients with "Phytid" Eruptions, *Arch Dermat & Syph* **29** 537 (April) 1934

3 Per, M I, and Braude, R. Contribution a la question de la valeur diagnostique et therapeutique de la trichophytine au cours de la dermatomycose a la lumiere des connaissances contemporaines sur l'allergie specifique et l'immunité, *Acta dermat-venereol* **9** 1, 1928

4 Traub, E F, and Tolmach, J A. Treatment of Dermatophytosis with Trichophytin, Convalescent or Immune Serum, and Vaccines, *New York State J Med* **39** 305, 1939

5 Lewis, G M, and Hopper, M E. An Introduction to Medical Mycology, Chicago, The Year Book Publishers, Inc, 1939, p 40

and allergy in fungous infections. It has seemed to us that a more systematic and correlated study of the fungistatic and fungicidal power of the blood serum should be attempted. This paper embodies a series of experiments with this point in view.

METHOD

More than 50 blood specimens from 35 patients were studied. The fungistatic action of the blood serum was determined by means of the "pellicle method," as described in previous publications.⁶ *Trichophyton gypseum* was the only micro-organism studied, not only because of its greater incidence as an infectious agent but also in order not to render the experiment more complicated. The same strain of *T. gypseum* was used throughout. The effects of the addition of 1, 10, 30, 50, 70 and 90 per cent concentration of blood serum to the Sabouraud bouillon on the growth of the micro-organism were studied. Adequate controls were made in each instance by comparing the growth of the fungi in plain Sabouraud bouillon.

The blood serum, in most instances, was used twenty-four hours after it was obtained, but it was placed in the ice box as soon as feasible after being drawn. In a few instances blood samples had to be transported for a few hours at approximately room temperature before the ice box could be reached. No preservative was added.

In using Sabouraud broth one has a convenient method of testing the fungistatic power of the various concentrations of blood serum on *T. gypseum*. It is possible to test the effects on this micro-organism because after the spores are inoculated in the depths of the fluid medium they first grow in the form of a cloudy suspension, thus growing under partially anaerobic conditions, and finally reach the top and form a pellicle. The degree of growth was measured both by the amount of subsurface flocculate and by the size of the surface pellicle.

If the different amounts of the serum were just added to the medium, there would result differing amounts of nutrient medium plus peptone in every tube. This factor of error was obviated in the following manner: The variable amounts of serum placed in the different tubes were diluted with distilled water until the fluid in each tube totaled 0.9 cc. To this was added 0.1 cc. of a tenfold concentration of Sabouraud broth, which had just been seeded with a measured quantity of the fungus being studied. In this way the final concentration of the medium was equal in each tube and always was equivalent to ordinary Sabouraud bouillon. The test tubes used averaged 1.25 cm. in diameter.

Complete coverage of the surface of the control tubes (containing only Sabouraud medium) by a pellicle took from six to nine days. The growth was more rapid in the summer. There was usually a good subsurface flocculate when there was a complete coverage of the surface by the pellicle, but in several instances when there was a wide pellicle completely covering the surface of the tube and even growing up on the sides of the tube there was only a moderate subsurface flocculate. In the tables a recording of 4 plus is made either when the pellicle completely covered the surface and showed a heavy subsurface flocculate or when there was a wide pellicle completely covering the surface with only a moderate amount of subsurface flocculate.

6. (a) Peck, S. M., and Rosenfeld, J.: The Effects of Hydrogen Ion Concentration, Fatty Acids and Vitamin C on the Growth of Fungi, *J. Invest. Dermat.* **1**:237, 1938. (b) Peck, S. M.; Rosenfeld, H.; Leifer, W., and Bierman, W.: Role of Sweat as a Fungicide, *Arch. Dermat. & Syph.* **39**:126 (Jan.) 1939.

Certain strains of *T. gypseum* seemed to be more resistant to the fungistatic power of blood serum than were others. To avoid this possible factor of error the same strain which was isolated at the beginning of this study was used throughout the experiments. It was noted that with continued subculturing even this strain gradually became somewhat more resistant to the fungistatic power of a serum than more recently isolated strains.

The fungistatic power of the blood serum manifested itself as a retardation in the rate of growth and as a limitation in the degree of growth of the micro-organisms during the fourteen days of observation as compared to the controls. A blood serum having marked fungistatic power would in many instances so injure the micro-organism that even after fourteen days it still lacked the ability to cover the surface of the medium completely with a wide pellicle. A serum having only moderate fungistatic power would so affect the micro-organism that there was a distinct lag in the rate of growth, but if it were observed for a long enough period eventually it would completely cover the surface of the medium with a wide pellicle.

RESULTS

Experiment 1—Fungistatic Power of So-Called Normal Serum

Ten persons, 6 men and 4 women, with a negative trichophytin reaction and no clinical evidence of dermatophytosis comprised a so-called normal group. All were adults between the ages of 20 and 55. An attempt was made to weed out of this group those who might have previously had dermatophytosis. For this reason a relatively small number of patients could be used as controls.

Growth of the micro-organism in the various concentrations of serum in bouillon at the end of six to fourteen days was indicated by plus signs, as given in the tables. In order to grade the fungistatic power of the blood serums, the effect on the growth of *T. gypseum* at the end of six to fourteen days of a 70 or 90 per cent concentration of the serum in Sabouraud bouillon was evaluated as follows:

(1) Strongly fungistatic serum	1 plus, 6 days, 1 or 2 plus, 14 days
(2) Moderately fungistatic serum	1 or 2 plus, 6 days, 2 or 3 plus, 14 days
(3) Slightly fungistatic serum	2 or 3 plus, 6 days, 4 plus, 14 days

In designating a serum as slightly fungistatic, growth of the fungi in the control tube had to show a greater acceleration of growth than the serum under investigation, even though growth in both was 4 plus at the end of fourteen days.

Table 1 summarizes the experiment. All experiments indicated that blood serum was fungistatic and not fungicidal. There was no instance of absolute inhibition of growth, even by the highest concentration of serum used. In only a few instances was the fungistatic power of the serum evident in concentrations below 30 per cent.

Only 1 blood serum (serum 9) showed absolutely no fungistatic power, 3 serums could be designated as slightly fungistatic, 2 could be rated as having moderate fungistatic power, and 6 could be designated as having strongly fungistatic power.

Two specimens of blood were taken from each of 2 patients in this series several months apart. It can be seen from table 1 that there was a variation in the fungistatic power of the blood samples from the same person. This variation in the fungistatic power of blood serum taken at various intervals from the same patients will be noted in subsequent experiments. It seemed to some extent to bear some relation to the time of year (summer or winter) when the blood was taken.

TABLE 1.—*Fungistatic Power* of Normal Serum (from Patients with No Evidence of Dermatophytosis and with Negative Trichophytin Reaction)*

Sex	Number	Growth Period, Days	Concentration of Blood Serum, per Cent						Control	Date of Inoculation
			1	10	30	50	70	90		
M	1	6	3+	3+	2+	2+	1+	±	3+	12/ 7/38
		14	4+	4+	4+	4+	1+	1+	4+	
M	2	6	2+	2+	1+	1+	1+	1+	2+	12/14/38
		14	4+	4+	4+	3+	3+	3+	4+	
M	3	6	3+	1+	1+	1+	1+	±	2+	12/28/38
		14	4+	3+	2+	2+	2+	1+	4+	
M	4	6	2+	2+	2+	2+	1+	1+	2+	12/30/38
		14	4+	4+	2+	2+	2+	1+	4+	
F	5	6	2+	2+	1+	1+	1+	±	2+	1/14/39
		14	4+	4+	2+	2+	1+	±	4+	
F	6	6	2+	2+	1+	1+	±	±	2+	1/14/39
		14	4+	3+	2+	2+	2+	1+	4+	
M	7	6	4+	4+	4+	2+	2+	2+	4+	2/ 6/39
		14	4+	4+	4+	4+	4+	4+	4+	
M	8	6	4+	3+	3+	2+	1+	1+	4+	5/ 4/39
		14	4+	4+	4+	4+	3+	2+	4+	
F	9	6	4+	4+	4+	4+	4+	4+	4+	5/23/39
		14	4+	4+	4+	4+	4+	4+	4+	
F	10	6	4+	4+	4+	4+	4+	3+	4+	5/23/39
		14	4+	4+	4+	4+	4+	4+	4+	
F	11	6	4+	4+	4+	4+	4+	3+	4+	5/23/39
		14	4+	4+	4+	4+	4+	4+	4+	
M	12	6	4+	4+	3+	3+	2+	2+	4+	6/30/39
		14	4+	4+	4+	4+	4+	4+	4+	

* 0, No growth; ±, slight growth below surface; 1+, moderate flocculate below surface; 2+, good subsurface growth, sometimes small colony on surface; 3+, partial covering of surface or as a band on side of tube with heavy subsurface flocculate; 4+, heavy growth of surface mycelium with heavy subsurface flocculate, or wide pellicle completely covering the surface and moderate subsurface flocculate.

Experiment 2.—Fungistatic Action of Blood Serum in Patients with Positive Trichophytin Reactions.

Table 2 gives an analysis of 18 patients, 15 men and 3 women, with positive trichophytin reactions of varying degrees. Among these were some with dermatophytids and others with clinical evidence only of dermatophytosis, while a third group showed a positive reaction to the trichophytin test but no clinical or microscopic evidence of fungous infection. They were grouped in the table under these three classifications. All were adults in approximately the same age group as the patients in table 1.

TABLE 2—*Fungistatic Power* of Blood Serum (from Patients with Positive Trichophyton Reaction)*

Sex	No	Growth Period, Days	Concentration of Blood Serum, per Cent							Date of Inoculation	Comment
			1	10	30	50	70	90	Control		
M	1	6 14	3+ 4+	3+ 4+	3+ 4+	2+ 3+	2+ 2+	2+ 2+	3+ 4+	12/14/38	T gypseum epidermophytosis epidermophytids on hands
F	2	6 14	2+ 4+	2+ 4+	2+ 4+	1+ 4+	1+ 4+	1+ 3+	2+ 4+	12/16/38	T gypseum clinical epidermophytosis, plus epidermophytids
M	3	6 14	2+ 4+	2+ 4+	3+ 3+	2+ 3+	1+ 2+	± 1+	2+ 4+	12/30/38	T gypseum epidermophytosis plus epidermophytids, persistent case responded to injections of trichophytin
M	4	6 14	3+ 4+	3+ 4+	2+ 4+	2+ 4+	2+ 4+	2+ 4+	4+ 4+	4/ 5/39	Epidermophytosis plus epidermophytids positive trichophytin reaction
M	5	6 14	4+ 4+	4+ 4+	4+ 4+	3+ 4+	3+ 4+	3+ 4+	4+ 4+	4/21/39	Acute epidermophytosis plus epidermophytids strongly positive trichophytin reaction, positive microscopically
M	6	6 14	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	6/16/39	Clinical epidermophytosis plus epidermophytids, trichophytin reaction strongly positive
F	7	6 14	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	6/28/39	Epidermophytosis plus epidermophytids trichophytin reaction strongly positive, positive microscopically
M	8	6 14	3+ 4+	3+ 4+	3+ 4+	3+ 4+	2+ 3+	1+ 2+	3+ 4+	12/ 7/38	No clinical evidence of epidermophytosis, slightly positive trichophytin reaction
M	9	6 14	3+ 4+	3+ 4+	2+ 4+	2+ 2+	1+ 2+	1+ 2+	3+ 4+	12/ 9/38	Clinical epidermophytosis
M	10	6 14	3+ 4+	3+ 4+	3+ 4+	2+ 4+	1+ 3+	1+ 3+	2+ 4+	12/14/38	Epidermophytosis of groin and toes, markedly positive trichophytin reaction
M	11	6 14	4+ 4+	4+ 4+	3+ 4+	3+ 4+	2+ 4+	2+ 4+	4+ 4+	2/15/39	Scaling between toes eczema of hands trichophytin reaction strongly positive
M	12	6 14	4+ 4+	4+ 4+	4+ 4+	3+ 4+	2+ 4+	2+ 4+	4+ 4+	6/30/39	Epidermophytosis
M	13	6 14	3+ 4+	3+ 4+	2+ 4+	2+ 4+	2+ 3+	2+ 3+	3+ 4+	12/ 7/38	No clinical evidence of epidermophytosis, positive trichophytin reaction
F	14	6 14	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	6/28/39	Dermatophytosis (?), markedly positive trichophytin reaction
M	15	6 14	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	8/ 9/39	No clinical signs of epidermophytosis
M	16	6 14	3+ 4+	3+ 4+	3+ 4+	3+ 4+	3+ 4+	3+ 4+	3+ 4+	1/18/39	Trichophyton purpureum, slightly positive trichophytin reaction
M	17	6 14	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4/ 5/39	Positive trichophytin reaction, involvement of hands and feet T purpureum
M	18	6 14	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4+ 4+	4/21/39	Positive trichophytin reaction involvement of hands and feet T purpureum

* 0, No growth, ±, slight growth below surface, 1+, moderate flocculate below surface 2+, good subsurface growth, sometimes small colony on surface, 3+, partial covering of surface or as a band on side of tube with heavy subsurface flocculate, 4+, heavy growth of surface mycelium with heavy subsurface flocculate, or wide pellicle completely covering the surface and moderate subsurface flocculate

The blood samples were graded as in the previous group. There were 6 patients whose blood serum showed no fungistatic power, according to our method of evaluation; the blood serum of 5 showed slight fungistatic power; that of 3 showed moderate fungistatic power, and that of 4 showed strong fungistatic power.

The blood serums of patients in this group showed no increased fungistatic power as compared with those in the first series of normal persons.

There were 7 patients with dermatophytids. Two showed no fungistatic power in their serum; 2 had slightly fungistatic blood serum; 2 had moderately fungistatic blood serum, and only 1 had strongly fungistatic serum. Our results were contrary to those of Ayres and Anderson² and resembled those of Lewis and Hopper.⁵

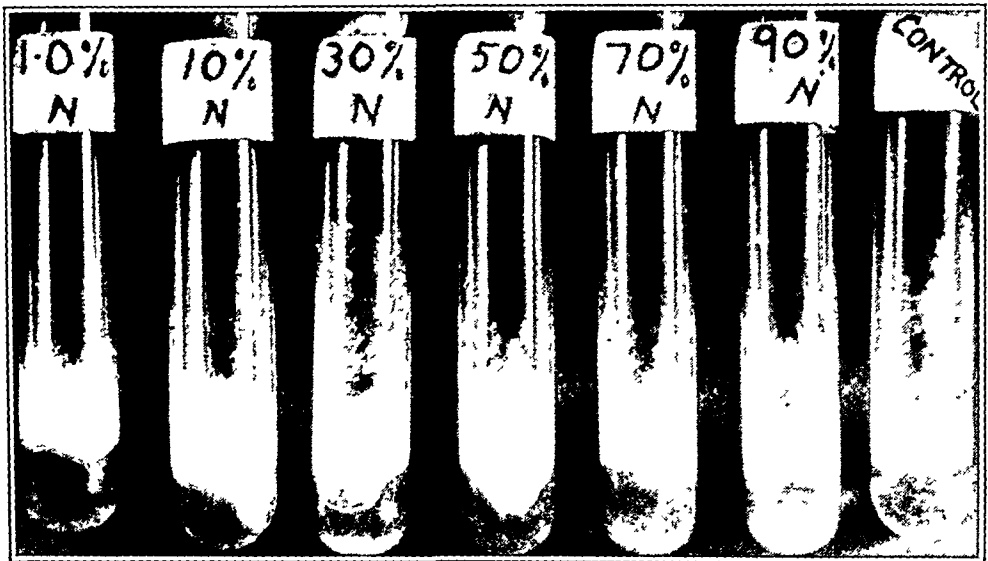


Fig. 1 (case 7, table 2).—Blood serum from a patient with dermatophytids and a strongly positive trichophytin reaction. Growth of *T. gypsum* fourteen days after inoculation. The serum showed no fungistatic power.

Too few cases were included in any subgroup to enable us to draw any definite conclusions. There were enough data on hand, however, to indicate that the strength of reaction to the trichophytin test bore no relation to the fungistatic power of a person's blood serum. One might deduce from these observations that the degree of fungous allergy or hypersensitivity bore no relation to the fungistatic power of the patient's serum.

Experiment 3.—Effect of Inactivation on the Fungistatic Power of Blood Serum.

An interesting observation was made while we were studying the effect of heat on the factors responsible for the fungistatic power of

blood serum It was seen in a few instances that if the blood serum was heated at 56 C for twenty minutes (as in the ordinary procedure for inactivation of serum for complement fixation reactions), there was an actual increase in the fungistatic power of the serum This increase in fungistasis after inactivation was found in only 6 of the 36 cases investigated

In contrast to this increase after heating for twenty minutes, heating the blood serum at 56 C for more than one hour usually decreased its fungistatic power An attempt was made in a series of experiments to identify complement with the factor responsible for the difference in fungistatic power of normal and inactivated serum, but this was not possible

An increase in fungistasis of the inactivated serum as compared with the unheated serum was found in only 1 of the control group (case 1, table 1) Four of the 6 cases were from those included in table 2 (cases 8, 9, 13 and 14)

None of the 6 cases were among those of dermatophytids This fact might be of importance The greatest increase in fungistasis following inactivation was observed in the serum of a patient who presented clinical and microscopic evidence of dermatophytosis but who had a negative reaction to a trichophytin test

Experiment 4—Effects of Injections of Trichophytin⁷ on the Fungistatic Activity of Normal and of Inactivated Serum

An attempt was made to determine the influence of the injections of trichophytin on the fungistatic power of the blood serum While it is as yet not clear just what the mechanism is which determines the amelioration of symptoms after injection of trichophytin, following the original report of Sulzberger and Wise,⁸ many observers now agree that there are a number of striking instances of excellent therapeutic results following the injection of trichophytin in cases of resistant dermatophytosis with dermatophytids

The commonly accepted theory is that by the injection of trichophytin a hyposensitization or desensitization is brought about, which then renders it impossible, or less likely, for the fungi or their products to elicit dermatophytids when coming in contact with the allergic skin

All observers agree with the report of Sulzberger and Wise⁸ that previously positive reactions to trichophytin tests can be made negative

7 A trichophytin made in our laboratory from *Trichophyton gypsum* was used in this experiment

8 Sulzberger, M B, and Wise, F Ringworm and Trichophytin, J A M A 99 1759 (Nov 19) 1932

by injections of trichophytin. It has been noted by us and by others⁴ that frequently after the injections were discontinued the trichophytin test gave positive reactions again. The accompanying case reports illustrate the effects of injections of trichophytin on the fungistatic power of blood serum in normal and in inactivated blood.

CASE 1.—*T. gypseum* was isolated from the lesions of the feet of a man with a negative reaction to a trichophytin test. There were no dermatophytids. Blood was taken at the start of the experiment. The patient was given an injection

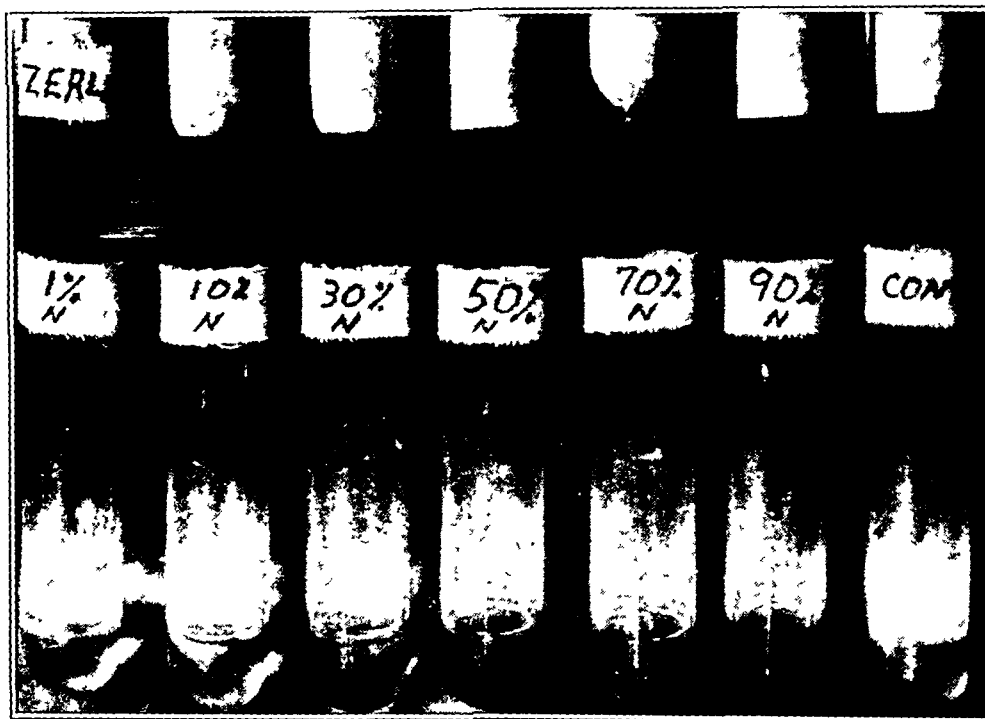


Fig. 2 (case 1, experiment 4).—Blood serum from a patient with a negative trichophytin reaction and dermatophytosis. Growth of *T. gypseum* eight days after inoculation. The serum was strongly fungistatic.

of trichophytin (1 cc. given subcutaneously) twice a week from the beginning of December 1938 to May 1939.

	Unheated Blood Serum ⁹	Heated Blood Serum ¹⁰
12/ 7/38	Strong fungistatic power	More fungistatic than unheated
12/30/38	Strong fungistatic power	More fungistatic than unheated
2/10/39	Moderate fungistatic power	No difference

9. The method of grading the serum was the same as used in experiments 1 and 2.

10. While unheated serum showed a 1 plus growth at the end of six days, the inactivated 90 per cent concentration of serum showed no growth; at the end of fourteen days there was a 2 plus growth in the 90 per cent concentration of unheated serum and only 1 plus in the heated serum.

CASE 2 (case 2, table 2) —In a patient with persistent dermatophytosis plus dermatophytids *T. gypsum* was isolated. A positive reaction to a trichophytin test was obtained on Dec 15, 1938. Injections of trichophytin were given three times a week. The patient was desensitized by the end of February. Injections of trichophytin were continued up to July 22, 1939.

	Unheated Blood Serum	Heated Blood Serum
12/16/38	Moderate fungistatic power	No difference
1/ 4/39	Moderate fungistatic power	No difference
1/18/39	Moderate fungistatic power	No difference
2/ 3/39	Moderate fungistatic power	No difference
4/21/39	Slight fungistatic power	No difference

CASE 3 (case 6, table 2) —A patient with dermatophytosis plus dermatophytids gave a strongly positive reaction to the trichophytin test. Trichophytin was injected from June 13 to July 25 twice a week, with decreased trichophytin hypersensitivity.

	Unheated Blood Serum	Heated Blood Serum
6/16/39	No fungistatic power	No difference
7/ 7/39	No fungistatic power	No difference
8/ 9/39	No fungistatic power	No difference

CASE 4 (case 14, table 2) —A patient with questionable dermatophytosis, who gave a markedly positive reaction to a trichophytin test, was treated from June 26 to August 9 twice weekly with injections of trichophytin, with reduction in sensitivity.

	Unheated Blood Serum	Heated Blood Serum
6/28/39	No fungistatic power	No difference
8/10/39	No fungistatic power	No difference

CASE 5 (case 12, table 2) —A patient received injections of trichophytin twice weekly from June 28 to August 9. By August 9 the patient was partially desensitized to trichophytin.

	Unheated Blood Serum	Heated Blood Serum
6/30/39	Slight fungistatic power	No difference
8/10/39	No fungistatic power	No difference

In these cases the injections of trichophytin did not increase the fungistatic power of the blood serum. On the contrary, in 3 cases the fungistatic power of the trichophytin-treated patients was apparently decreased.

Case 2 was an example of the lack of relation between the fungistatic power of the blood serum and the clinical symptoms. This patient was clinically improved after the injection of trichophytin. The dermatophytids which were present on the hands practically disappeared. However, with the improvement of the clinical symptoms, the fungistatic power of the blood serum seemed to be decreased. In December, when the first specimen of blood was taken, there were vesicular dermatophytids plus eczematization of the hands and a frank dermatophytosis. In March she was much improved. At that time the fungistatic power of the blood serum was at its lowest level, as far as could be determined from our experiments.

We can thus conclude that injections of trichophytin did not increase the fungistatic power of the blood serum. Our results seemed to substantiate the conclusions of Per and Braude,³ who maintained that injections of trichophytin decreased the fungistatic power of serum. The effects of inactivation of the serum on the fungistatic power of blood serum were not influenced by the injections of trichophytin.

Experiment 5.—The Fungistatic Power of Guinea Pig Serum.

The blood serum of guinea pigs was also investigated for its fungistatic power.

		Pooled Serum Unheated Blood Serum	Heated Blood Serum
1/21/39	2 pigs	Strong fungistatic power	Moderate fungistatic power
1/27/39	2 pigs	Strong fungistatic power	Strong fungistatic power
4/13/39	2 pigs	Strong fungistatic power	Moderate fungistatic power
5/ 8/39	2 pigs	Slight fungistatic power	Slightly increased fungistatic power

It will be noted that the guinea pig serum was fungistatic. It followed practically the same rule as did the human serum; that is, the fungistatic power was first noted in about a 30 per cent concentration of guinea pig serum in Sabouraud bouillon, with a gradual increase in fungistasis with increase in the concentration. The blood serum even in a 90 per cent concentration was fungistatic and not fungicidal.

Experiment 6.—The Fungistatic Power of Vesicle Fluid.

Vesicle fluid from 2 patients with dermatophytosis and dermatophytids was tested for fungistatic power. The fluid was obtained from vesicles on the hands in order to test, if possible, only dermatophytids. The roof of such vesicles was cultured, and in no instance was it possible to obtain a growth of fungi. The vesicle fluid was found to be less fungistatic than a comparative concentration of blood serum from the same person. The fungi grew readily in a 100 per cent concentration of vesicle fluid from both patients.

For control studies blood was obtained from a child with epidermolysis bullosa, and vesicle fluid was obtained from a traumatic vesicle on the child's hand. As can be seen from figure 3, while the 90 per cent concentration of blood serum from this patient in Sabouraud bouillon was practically not fungistatic, the vesicle fluid showed a marked inhibitory effect on the growth of the fungi.

Ascitic fluid was used instead of blood serum in a number of experiments and was found to have a moderate degree of fungistasis.¹¹

11. This work was done with the technical assistance of Edward Weissbard.

SUMMARY AND CONCLUSIONS

The fungicidal and fungistatic power of human blood serum was tested by means of the pellicle method with *T. gypseum* in Sabouraud bouillon. Examination of more than 50 samples of blood from 35 persons indicated that blood serum is fungistatic.

The fungistatic power of the blood serum usually first became evident in a 30 per cent concentration of serum in Sabouraud bouillon. There was a gradual increase of fungistasis in the higher concentrations.

Twelve samples of blood serum from 10 control patients were examined. Of these, 1 showed no fungistatic power, 3 could be classified as slightly fungistatic, 2 could be rated as having moderately

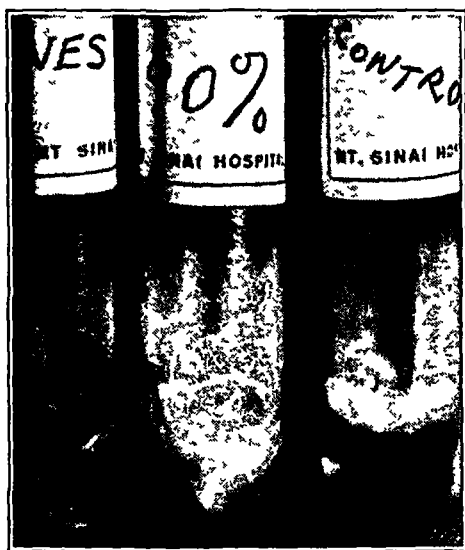


Fig. 3—Specimens from a patient with epidermolysis bullosa. Strong fungistatic action of vesicle fluid (tube at the left), as compared with the action of 90 per cent concentration of blood serum from the same patient (center tube). The tube at the right is a control.

fungistatic power, and 6 were found to have strong fungistatic power, according to the method of grading previously described.

Eighteen samples of blood from 17 patients with positive trichophytin reactions of varying intensities were also investigated for their fungistatic action. Among these patients, there were 7 with dermatophytids and others with clinical and microscopic evidence of dermatophytosis but no dermatophytids, while a third group showed positive reactions to trichophytin tests but no clinical or microscopic evidence of fungous infection.

Of this group of serums 6 had no fungistatic power, 5 were slightly fungistatic, 3 were moderately fungistatic and 4 were strongly fungistatic. Of the 7 patients with dermatophytids, 2 showed no fungistatic power

in their serums; 2 had slightly fungistatic power in their serums; 2 had moderately fungistatic power, and the blood serum of 1 could be graded as strongly fungistatic.

Our experiments seemed to indicate that while blood serum may have fungistatic power, there is no increase in fungistasis in patients who have dermatophytids as compared with so-called normal controls. There is no relation between the degree of fungistasis and the strength of reaction to the trichophytin test.

Inactivation of the blood serum, heated at 56 C. for twenty minutes, caused an increase in fungistasis in 6 samples of serum of a total of 35 examined.

Injections of trichophytin seemed either to have no effect on the fungistatic power of blood serum or in some instances to decrease it.

Guinea pig serum has fungistatic power. Ascitic fluid was found to be only moderately fungistatic.

Vesicle fluid from dermatophytids failed to show any fungistatic action. However, fluid from vesicles from a patient with epidermolysis bullosa showed a strong fungistatic action, although the blood showed none.

PENIFORM ELEPHANTIASIS OF THE PRAEPUTIUM CLITORIDIS IN LYMPHOGRANULOMA VENEREUM

WALDEMAR E COUTTS, M D

AND

OLGA MONETTA, M D

SANTIAGO, CHILE

Lymphogranulomatous syndromes of the female external genitalia have been well studied and classified by different authors. Simple chronic ulcers of the vulva, anterior genital elephantiasis (labia majora), with or without ulcerations, and the complex denominated esthiomene, with or without anorectal complications, constitute the best known forms of the disease.

For some years we have had the opportunity of examining and following the evolution of one or another of the aforementioned manifestations in prostitutes. Among these women we have observed a special form of elephantiasis, which affects principally the covering of the clitoris and which we have designated "peniform hypertrophy of the praeputium clitoridis," owing to the aspect that this manifestation presents in its most advanced stages.

This syndrome is not common, in only 5 of 66 women (7.5 per cent) presenting elephantiasis vulvae of a lymphogranulomatous nature have we been able to establish its presence and find different stages of its evolution.

The initial stage of this syndrome is characterized by a varying degree of elephantiasis of the labia majora and a slight hard edematous infiltration of the glans clitoridis and its prepuce. The clitoris and prepuce appear like the knob of a bell lying between the infiltrated labia majora (fig 1 A). In a more advanced stage, the hypertrophied parts protrude between the labia majora and hang downward (fig 1 B). Such a formation is covered on its outer surface by skin and posteriorly by mucosa. It is of hard consistency, which is more marked at the distal and free extremity. The root of the structure preserves a softer consistency. In the final stages the structure hangs before the external genitalia like a penis and completely covers the urethral and vaginal orifices (fig 2).

In the intermediate and advanced stages of the syndrome the posterior surface of the peniform structure appears ulcerated and macerated owing to secondary infections favored by the constant irritative action of

From the Department of Social Hygiene, Public Health Service

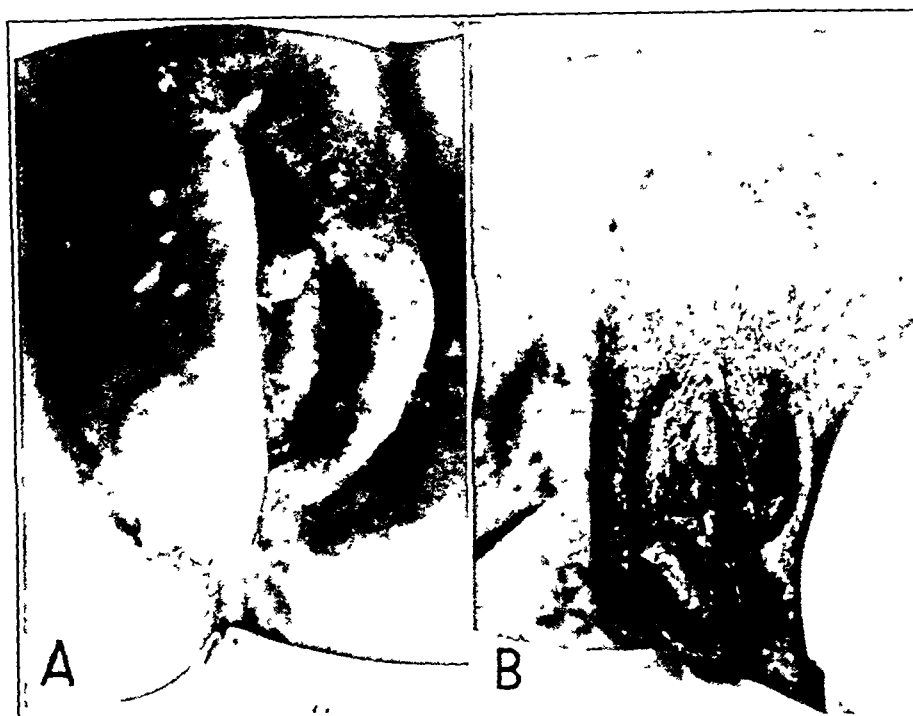


Fig. 1.—Elephantiasis of the prepuce of the clitoris: *A*, as a small knob between the labia majora, and *B*, in a more advanced stage.



Fig. 2.—Advanced stage of elephantiasis of the prepuce of the clitoris.

the urine In the longest-standing case of our series (four years), represented in figure 2, we were able to establish the existence of papular formations on the posterior surface and free extremity, the aspect of which was much like that of so-called "pseudo-lues papulosa," described by Lipschutz

Maceration of tissues of this pendular structure and secondary infection contribute to give the condition a foul odor Dark field examination of the soggy material that covers the posterior surface reveals the existence of enormous numbers of spirochetes

Specimens removed for biopsy from 2 of our patients and stained, after fixation in Susa's or Mingazzin's solution, by Mann's procedure showed the existence of numerous cytoplasmic and free microscopic and macroscopic granulocorpuscles of the type described by Miyagawa¹ in experimental lymphogranulomatous lesions and by Coutts, Martini and Gacitua² in different human structures attacked by the virus of the disease

In the presence of this syndrome, in which a preeminence of the elephantiasic process resides in the praeputium clitoridis, several conjectures may be made on the basis of clinical and anamnestic data

All recorded cases of our series were among prostitutes of the lowest social class All of them had noticed as a first manifestation of the disease an increase in size of one or both labia majora The study and analysis of lymphatic circulation of the region, as demonstrated in the textbooks of Testut and Cunningham and in the specialized treatise on lymphatics by Rouvière,³ do not throw any light on the preeminence of periclitoredean hypertrophy Lymph node stasis in determined territories, the circulation of which is not yet well known, would be the only possible explanation for this phenomenon

Careful observation of our cases has shown that the clitoris, especially the glans, partakes in the process at its earliest period Later involvement of this structure in the diseased tissues does not allow us to establish its definite participation Surgical removal of the pendular portion and a careful search for erectile tissue would clear the problem up definitely as regards this point Unfortunately, our patients have not permitted surgical intervention

Vicuña Mackenna 35 A

Carmen 226

1 Miyagawa, Y On the Virus of Lymphogranuloma Inguinale, *Jap J Dermat & Urol* **39** 105, 1936

2 Coutts, W E, Martini, J, and Gacitua, M Entwicklungsformen des Virus des Lymphogranuloma Inguinale, *Dermat Wchnschr* **107** 1404, 1938

3 Rouviere H Anatomie des lymphatiques de l'homme, Paris, Masson & Cie, 1932

ERYTHEMA ELEVATUM DIUTINUM

REPORT OF A CASE

FRANK C. COMBES, M.D.

AND

SAMUEL M. BLUEFARB, M.D.

NEW YORK

The nosologic position of erythema elevatum diutinum (persistent elevated erythema) is still uncertain. Over ten years ago Weidman and Besancon¹ made an admirable attempt to prove its identity, isolating an organism (*Streptococcus ignavus*) and divorcing the condition from granuloma annulare and the erythema multiforme perstans group of cutaneous diseases. Crocker and Williams,² Trimble³ and Gray⁴ also considered it a separate entity. Trimble and Weidman and Besancon felt sympathetic to the hypothesis that the so-called Bury type and granuloma annulare were the same but nevertheless recognized the Hutchinson type as existing separate and distinct from granuloma annulare.

We agree with Weidman and Besancon that the sparsity of cases appearing in the literature has made it impossible to collect sufficient data to determine the clinical and histologic requisites for diagnosis of this rare disease.

The patient on whom this report is based was admitted to Bellevue Hospital in January 1938. Reports based on him have previously appeared in the literature, with tentative diagnoses of lymphoblastoma, xanthoma,⁵ mycosis fungoides,⁶ multiple idiopathic hemorrhagic sar-

From the Department of Dermatology and Syphilology, New York University College of Medicine, and the Department of Dermatology and Syphilology, Third Medical (New York University) Division, Bellevue Hospital, service of Dr. Edward R. Maloney.

1. Weidman, F. D., and Besancon, J. H.: Erythema Elevatum Diutinum, *Arch. Dermat. & Syph.* **20**:593 (Nov.) 1929.

2. Crocker, H. R., and Williams, C.: Erythema Elevatum Diutinum, *Brit. J. Dermat.* **6**:1 (Jan.) 1894.

3. Trimble, W. B.: Erythema Elevatum Diutinum: Report of a Case, with Remarks on Its Nosologic Position, *Arch. Dermat. & Syph.* **13**:383 (March) 1926.

4. Gray, A. M. H.: A Case of Erythema Elevatum Diutinum, *Brit. J. Dermat.* **44**:551 (Nov.) 1932.

5. Bloom, D.: A Case for Diagnosis (Lymphoblastoma? Xanthoma?), *Arch. Dermat. & Syph.* **37**:918 (May) 1938.

(Footnotes continued on next page)

coma⁷ and erythema elevatum diutinum⁸ It is interesting to note that a diagnosis of granuloma annulare was never advanced

REPORT OF CASE

J H, a white man aged 64, when first seen had an eruption of five months' duration His past history was not significant He stated that he had not had syphilis or gonorrhea Furthermore, there was no history of the ingestion of drugs which might have been responsible for the lesions

The eruption appeared on his neck in September 1937 and was not accompanied by subjective sensations The rest of the lesions appeared within the following two months They were generalized and consisted of variously sized nodules and plaques, ranging from 0.5 to 4 cm in diameter There was some tendency toward grouping, especially around the joints Small aggregate lesions were present about his ears and nose On both sides of his neck posteriorly were clumps of slightly larger lesions Similar isolated ones were situated on his chest and back On the extremities there was a tendency toward localization, especially about the wrists and even on the knuckles and dorsum of the proximal articulations of the fingers The mucous membranes were not involved All of the lesions appeared similar in their general characteristics They were circular or irregularly oval, arising abruptly from the normal skin The larger ones were plateau-like, while in the others the centers were perceptibly more elevated than the edges In none was there any evidence of central depression or regression They varied from dusky reddish brown in the larger to orange yellow in the smaller ones Those about the neck might readily have been mistaken for xanthomas The surface of all was smooth and devoid of crust and scale The normal cutaneous markings were less distinct than on the surrounding skin Lanugo hair was absent from the surface of the nodules On palpation the nodules were firm and densely infiltrated and did not seem to encroach beyond their visible borders but could be lifted freely from the subcutaneous tissue

The patient was well developed, well nourished and apparently in good health His pupils were normal His teeth and gums were in poor condition There was no adenopathy except in the inguinal region, where he had a few tender glands about the size of a hazelnut The lungs were normal except for slight wheezing heard at the bases, with some diminution of breath sounds The heart sounds were somewhat diminished, and there was a systolic murmur at the apex The borders were within normal limits No mass, tenderness or rigidity was felt in the abdomen The liver, spleen and kidneys were not palpable The extremities were normal but for a bilateral hallux valgus No pathologic reflexes were present

The tuberculin test (Mantoux) gave a negative reaction with 1 to 100,000 dilution but a 3 plus reaction with a 1 to 1,000 dilution The urine was normal The Wassermann reaction of the blood was negative Clinical and cytologic

6 Fox, H A Case for Diagnosis (Mycosis Fungoides? Lymphoblastoma?), *Arch Dermat & Syph* **38** 103 (July) 1938 Bloom, D A Case for Diagnosis (Mycosis Fungoides?), *ibid* **38** 124 (July) 1938

7 Bloom, D A Case for Diagnosis (Kaposi's Sarcoma?), *Arch Dermat & Syph* **38** 472 (Sept) 1938

8 Bloom, D Erythema Elevatum Diutinum, *Arch Dermat & Syph* **39** 369 (Feb) 1939

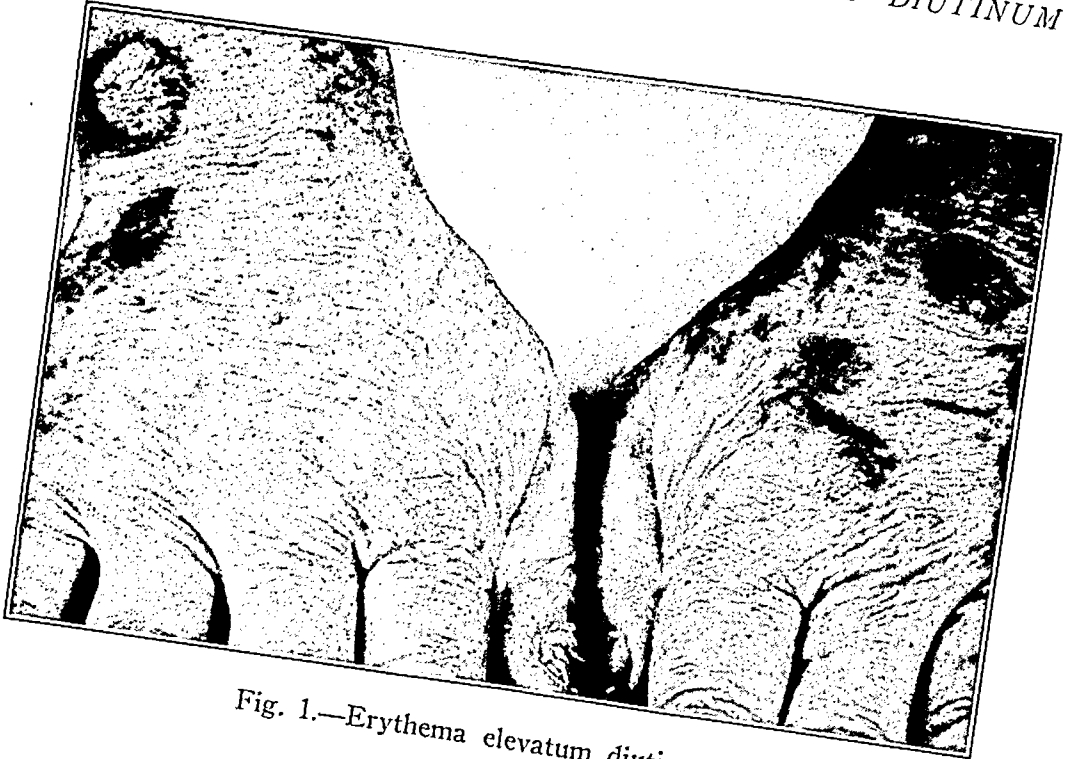


Fig. 1.—Erythema elevatum diutinum.



Fig. 2.—Erythema elevatum diutinum.

examination of the blood showed no abnormalities except slight excess of free cholesterol esters (117 mg per hundred cubic centimeters) Roentgenograms showed no pathologic changes in the lungs or bones Several smears taken by sternal puncture showed the elements of bone marrow to be normal

Sections of the nodules were examined histologically The epidermis showed acanthosis The underlying corium was granulomatous, showing a profuse infiltration of small and large round cells, many polymorphonuclear leukocytes, fibroblasts, occasional epithelioid cells and numerous eosinophils In the stroma there was a well defined hyperplasia of the spindle cells A subacute inflammatory process existed about the blood vessels, and there was hyperplasia of the vessels, with toxic necrosis of their walls This hyperplasia was so intense that some of the lining endothelial cells were gigantic The fibrils were more or less granular

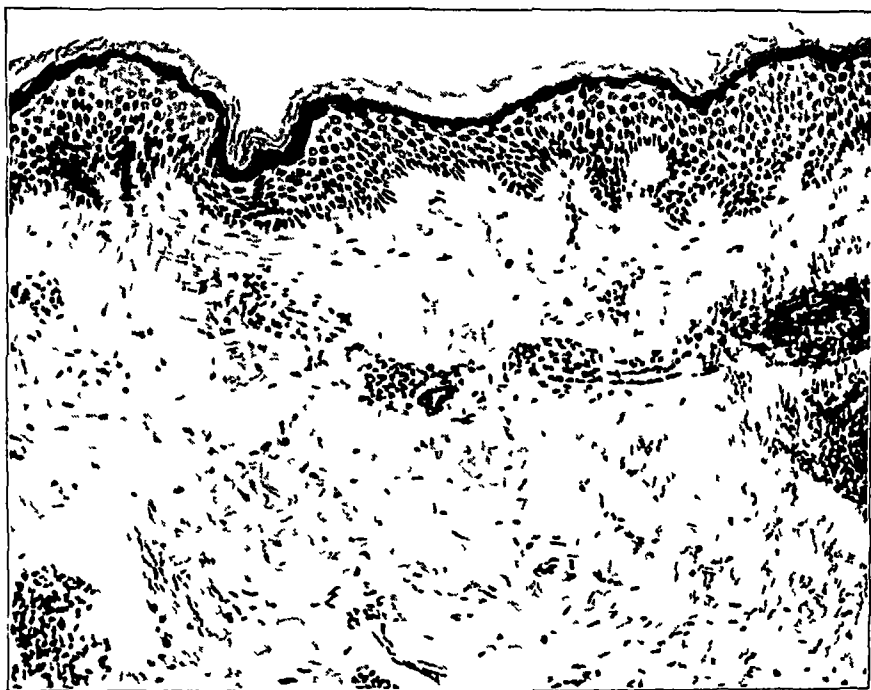


Fig 3—Low power photomicrograph of tissue from lesion on the leg

and degenerated and took the eosin stain more strongly than normal Some of the vessels were more or less completely occluded, although there was no thrombosis The nuclei of the endothelial cells were pyknotic, and occasional polymorphonuclear leukocytes were seen within them

COMMENT

On the basis of histologic studies, Weidman and Besancon¹ stated the belief that erythema elevatum diutinum was the cutaneous expression of a bacteremia, distinct from granuloma annulare They were able to isolate *Str ignavus* from the lesions After a careful study they concluded

"The major pathologic changes may be gathered and interpreted under two headings (1) an acanthosis in the epiderm and (2) an acute toxic periarteritis

and peritelangiitis in the corium. The acanthosis was not of the most extreme grade possible, being rated as grade II in this laboratory. The excessive thickening of the stratum corneum must be due in greatest part to rubbing on such exposed positions as are concerned in this dermatosis; but, in view of the intensity of the toxic changes observed deeper, we believe that these at least add to the mechanical factors, if there are such in the case, although no infiltration of leukocytes could be seen actually within the epiderm.

"As to the acute exudative feature in the corium, this was fully as acute a process as that of erysipelas, but showed damage to the blood vessel walls . . . in a much more definite way than in erysipelas. The extremeness of the toxic hyaline change seen in the older lesions is, in our experience, pathognomonic, but we must at once emphasize that reliance must not be placed on this alone for diagnosis. . . .

As far as we know, this is the only dermatosis (of the skin proper) in which masses of polymorphonuclears dominate the picture, apart from such severe acute fulminating conditions as erysipelas, cellulitis and perhaps erythema nodosum."

Most of the confusion in reference to the existence of this condition distinct from granuloma annulare seems to have arisen as a result of the article written by Crocker and Campbell Williams. Unfortunately they included under the name of erythema elevatum diutinum a case described by Bury⁹ in 1889, which was probably one of granuloma annulare, with Hutchinson's¹⁰ "purple patches of the skin." Graham Little¹¹ in 1908, in making a survey of the subject, concluded that erythema elevatum diutinum was a subvariety of granuloma annulare; but the cases he collected from the literature were of the so-called Bury type. His observations and conclusions have been of great value in clarifying the identity of this obscure condition. However, in 1932 in a discussion of a case presented by Gray, Graham Little¹² considered that the disease differed from granuloma annulare in the absence of discrete nodules. This difference between erythema elevatum diutinum and granuloma annulare was concurred in by Goldsmith.¹³

CONCLUSIONS

From our case report and a review of the literature, we agree with those who favor the hypothesis that erythema elevatum diutinum is a

9. Bury, J. S.: A Case of Erythema with Remarkable Nodular Thickening and Induration of Skin, Associated with Intermittent Albuminuria, *Illust. M. News* **3**:145, 1889.

10. Hutchinson, J.: On Two Remarkable Cases of Symmetrical Purple Congestion of the Skin in Patches with Induration, in *Lectures on Clinical Surgery*, London, J. & A. Churchill, 1878, vol. 1; *Brit. J. Dermat.* **1**:10, 1888-1889; *Arch. Surg.* **1**:372, 1890-1891.

11. Little, E. G. G.: Granuloma Annulare, *Brit. J. Dermat.* **20**:213 (July) 1908.

12. Little, E. G. G., in discussion on Gray.⁴

13. Goldsmith, W. N., in discussion on Gray.⁴

distinct clinical entity We believe that the Bury type does not exist but is actually a variant of granuloma annulare We have tabulated the predominant reasons for our conclusions in the accompanying tabulation

	Erythema Elevatum Dutinum	Granuloma Annulare
Distribution	Bilateral and roughly symmetric	Unilateral
Age and sex	Middle aged and elderly men	In children and young women
Lesion	Flat, raised and red, with no central clearing	Colorless or pink ring of nodules, with usually normal center
Duration of lesions	Persistent	Fade and reappear
Response to treatment	Usually radioresistant	Radiosensitive
Histologic observations	Preeminently acute (in terms of tissue process) polymorphonuclear leuko cytes and eosinophils but not necrosis	Process varies from subacute to chronic, with fibroblastic prolifera tion as the predominant reactive expression and extensive necrosis

Dr Frederick Weidman and Dr Timothy J Riordan furnished the histologic interpretation

PYODERMA CHANCRIFORME FACIEI

GAROLD V. STRYKER, M.D.

ST. LOUIS

Under the title of isolated chancre-like pyoderma of the skin of the face (pyoderma chancriforme faciei), Hoffmann¹ reported 5 cases of almost identical lesions which appeared as single foci on the face. The lesion in each case resembled a button-like, eroded or ulcerative chancre or vaccinia. The base was indurated and superficial (rarely deep), with smooth ulceration and without a separating border. The secretion was serous rather than purulent. The thin, elevated border was bright red, and the crusts were yellowish or darker. There was a hard, almost indolent swelling of the regional lymph gland. In 1 case a lesion identical in character with the original appeared symmetrically eleven months later on the opposite eyelid.

The ulcers occurred most commonly on soft skin, where irritation or maceration by tears or sputum might favor development. There were no important subjective symptoms. The lesions responded to antiseptic applications.

The laboratory findings, except a pure culture of *Staphylococcus aureus*, were normal. The histologic changes were reported as acanthosis, edema, distended lymph and blood vessels, toxic endovasculitis of the small veins and arteries, perivascular infiltration of lymphocytes, leukocytes, eosinophils and plasma cells. There were also fibroblasts and pigment-containing cells.

REPORT OF A CASE

R. H. E., a widow aged 50, a patient of Dr. Earl Brand, of Webster Groves, Mo., consulted me in December 1939 on account of an ulcer just below the outer canthus of the left eye. The lesion, which appeared suddenly and without premonitory symptoms, was pinhead sized at onset and enlarged in three and one-half weeks to a diameter of 1.5 cm.

Inspection revealed a round, shallow ulcer with a grayish yellow base, sloping edges, an elevated, hard, bright red border and a narrow areola of erythema. There was a thin, slightly purulent discharge. The lesion, which could be picked up, button-like, between the fingers, was freely movable over the subcutaneous tissue. The left preauricular lymph gland was enlarged, hard and slightly tender. There was no pain, burning or itching, and the temperature remained normal.

From the Department of Dermatology and Syphilology, St. Louis University School of Medicine.

1. Hoffmann, E.: Isolierte schankerähnliche Pyodermie der Gesichtshaut (Pyodermia chancriformis faciei), Arch. f. Dermat. u. Syph. **170**:403, 1934.

The patient had been in good health. She stated that she had never had a similar condition or any other cutaneous disease. Her normal weight had been maintained. There had been no recent respiratory or gastrointestinal disease or other illness. The physical examination gave essentially negative results. The death of her husband had caused frequent spells of crying over several weeks immediately prior to the appearance of the ulcer. This wetting of the skin by secretion was mentioned by Hoffmann as a possible predisposing factor.

Four weeks after the onset of the first lesion, a similar one appeared on the upper right eyelid. Its development was accompanied by slight burning. The clinical appearance was identical with that of the original lesion except that it did not attain a size larger than 5 mm in diameter.

Laboratory Findings—The dark field examination gave negative results. The Kahn reaction of the blood remained negative on repeated examination over two and one-half months after the lesion first appeared. The blood count showed 5,782 white cells and 5,020,000 red cells per cubic millimeter and 71 per cent



Fig 1—Pyoderma chancriforme faciei

hemoglobin. A differential count showed 28 per cent lymphocytes, 59 per cent segmented neutrophils, 2 per cent stab neutrophils, 2 per cent eosinophils, 1 per cent basophils and 8 per cent monocytes. Agglutination tests of the patient's blood serum gave negative results for tularemia and brucellosis. A pure growth of *Staph aureus* was obtained on culture.

Histologic examination of the tissue obtained from the hard edge of the ulcer showed acanthosis, edema of the papillary layer and cutis and vascular and lymphatic dilatation. A closely packed perivascular infiltrate was made up of leukocytes, lymphocytes, plasma cells and fibroblasts, with an occasional eosinophil. The infiltrate stopped abruptly just beyond the acanthotic epidermal border but extended from the papillary layer into the subcutis. There was no evidence of tuberculosis or carcinoma, and no fungi were found.

As diagnoses of chancre, carcinoma, tuberculosis, tularemia, vaccinia and sheep pox were ruled out by the history or by the results of laboratory procedures, there remained only the possibility of a pyogenic ulcer. This contention was supported by the growth of a pure culture of *Staph aureus*, the histologic observations and the response to treatment.

Treatment with crystal violet and with antiseptic packs was then instituted. Some improvement occurred at first. This was followed by an exacerbation, with increase of secretion and widening of the ulcers. Sulfamethylthiazole (2-sulfanil-amido-4-methylthiazole) (16 Gm. in twenty-four hours) was administered by mouth. Because it caused severe nausea, administration of the drug was discontinued. After seventy-two hours a smaller dose (12 Gm. per twenty-four hours) was employed for two days. Healing occurred at once in both lesions.

The indurated border of the original lesion underwent involution slowly and remained as a thin, elevated line about the scar for nearly two weeks after healing had occurred. The final scar was smooth, soft and without pigmentation.

In the light of Hoffmann's experience, healing could have been expected with ordinary antiseptics directed toward the staphylococci. In this instance, the use of sulfamethylthiazole appears to have hastened the final outcome.

EHLERS-DANLOS SYNDROME

JACOB SKEER, M D

AND

ARTHUR A KAPLAN, M D

BROOKLYN

The Ehlers-Cohn-Danlos¹ syndrome was until recently considered uncommon in America Tobias² reported the first case in the United States in 1934 In the last few years cases have been reported with increasing frequency The syndrome is characterized by excessive fragility of the skin and the blood vessels, hyperelasticity of the skin, hyperflexibility of the joints and the formation of pseudotumors and subcutaneous nodules

REPORT OF A CASE

A R, a white boy aged 3 years, was admitted to the pediatric ward of the Brooklyn Jewish Hospital, with the complaint of excessive bruising and bleeding The family history was irrelevant The child was born prematurely, in the thirty-second week of gestation, and weighed only 2½ pounds (1.15 Kg) at birth It was necessary to give him two transfusions of blood for weakness and cyanosis His development was then normal He had a cervical abscess when he was 1 year old, and the tonsils and adenoids were removed when he was 2 years old

The present condition was noted when the child began to walk, at approximately 14 months of age He suffered bruises easily, and ecchymosis developed after slight trauma Open wounds bled excessively and required tight dressings to produce hemostasis He did not have any spontaneous hemorrhages, nor was bleeding from the mucous membranes noted at any time

The child was friendly, well nourished and well developed The positive findings were limited to the skin and joints The skin was dry and scaly and showed cutis anserina on the extensor surfaces of the arms and legs When it was picked up it felt smooth and velvety It was loose and decidedly hyperelastic Manipulation of the joints showed a moderate degree of hyperflexibility, most noticeable in the fingers The muscles were somewhat flabby There were linear, irregularly shaped

From the Department of Dermatology and Syphilology and the Department of Pediatrics of the Jewish Hospital of Brooklyn

Presented before a meeting of the Section of Dermatology and Syphilology of the New York Academy of Medicine, Dec 16, 1939

1 Ehlers, E Cutis laxa, *Dermat Ztschr* 8 173, 1901 Cohn, P Demonstration eines Patienten mit Gummihaut (Cutis laxa) und eigentümlichen zirkumskripten Hautveränderungen, braunroten eindruckbaren Erhebungen, *Verhandl d deutsch dermat Gesellsch* 9 415, 1907 Danlos, H Un cas de cutis laxa avec tumeurs, *Bull Soc franç de dermat et syph* 19 70, 1908

2 Tobias, N Danlos' Syndrome Associated with Congenital Lipomatosis, *Arch Dermat & Syph* 30 540 (Oct) 1934

and atrophic scars of various sizes on the forehead, right cheek, back, elbows and knees. They were flat, somewhat depressed, wrinkled and papyraceous. The scar on the right side of the neck was the site of an operation for abscess. The linear scar on the left tibial region was caused by the removal of tissue for biopsy.

There were irregularly shaped, soft, multilobular, violaceous, raisin-like tumors and subcutaneous nodules on the elbows and knees. The patient struck his left elbow against a chair July 18, 1939. Following the trauma there were severe ecchymosis and a gaping wound in the skin, which bled profusely. The mother applied dressings but could not stop the bleeding. The patient was brought to the Jewish Hospital, and the hemorrhage was stopped. A ballooning red tumor formed,



Fig. 1.—Note atrophic scars on the forehead and the left elbow. There is a large pseudotumor on the right elbow.

which was subsequently absorbed after the application of tight dressings. The resultant atrophic scar was wide, flat and fanshaped, with radiating lines (fig. 1).

Laboratory Examination.—The hemoglobin content was 81 per cent; the erythrocytes numbered 4,300,000 and the leukocytes 13,000 per cubic millimeter. The differential count showed 40 per cent polymorphonuclear cells, 16 per cent eosinophils, 40 per cent lymphocytes and 4 per cent mononuclear leukocytes. There were no pathologic cells. The bleeding time was one minute, and the clotting time, seven minutes. The clot retraction time was eight hours, with a normal clot. The bone marrow confirmed the peripheral eosinophilia. The urine was normal. Roentgenograms of the long bones and of the lungs showed no abnormalities. The Kline and Mantoux tests gave negative results. Chemical examination of

the blood showed total lipids 587 mg, total cholesterol 203 mg, with free cholesterol 28 per cent, and calcium 112 mg per hundred cubic centimeters, the phosphorus content was 46 mg and the value for phosphatase 169 Bodansky units. Chemical examination of the skin showed total solids 52.4 per cent, total lipids 32.1 per cent (of dry weight) and total cholesterol 0.48 per cent (of dry weight). The percentage of free cholesterol was too low to determine.

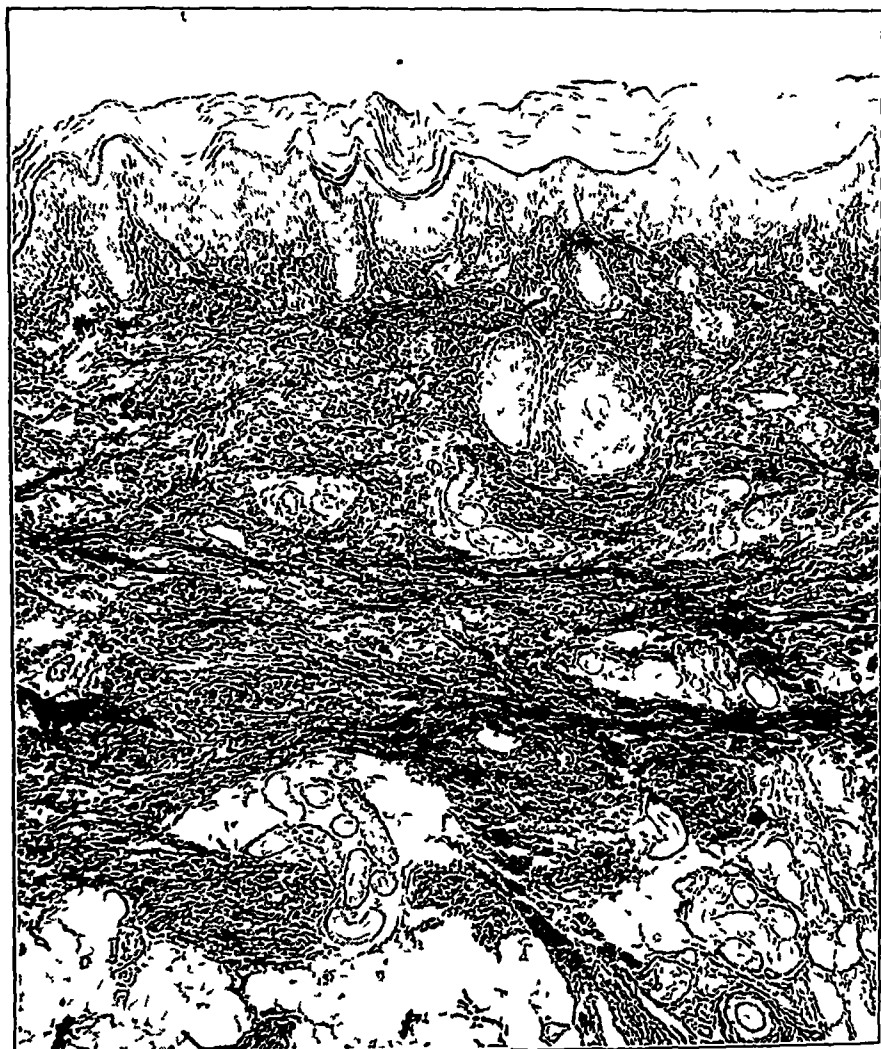


Fig 2—The epidermis is wavy. The dense network of elastic fibers fills the papillary bodies and extends to the midcutis (Weigert's elastic tissue stain, $\times 100$).

The results of microscopic examination of the tissue removed from the left tibial region were reported by Dr D L Satenstein as follows:

With the hematoxylin and eosin stain the framework of the subepidermal cutis was dense, the fibers in the papillary bodies were heavy. In the midcutis there was considerable irregularity in the thickness of the fibers, which in part were arranged parallel with the surface. The usual network of the cutis was not present. The blood vessels were not telangiectatic, and the adnexa were normal.

With Weigert's elastic tissue stain the picture was striking. The subepidermal network of elastic fibers was extremely dense, almost filling the papillary bodies and extending down to the upper part of the middle portion of the cutis. The fibers in the middle part of the cutis were increased in amount and appeared in part as a network around the individual collagen bundles. There was no increase of elastic tissue about the vessels or adnexa, and it was somewhat sparse in the subcutis (fig. 2).

Under high power the elastic fibers were seen to extend into the epidermis between the basal cells; they were thicker than usual in this zone. In the upper part of the cutis there was considerable variation in the thickness of the fibers. There was considerable breaking up of fragments of various sizes. In the deep part of the cutis the fibers were thick and somewhat wavy and were arranged parallel with the surface. There was no evidence of activity or degeneration.

To summarize, there were extensive hyperplasia and thickness of the elastic tissue throughout the cutis, most pronounced in the upper part. The microscopic diagnosis was hyperplastic elastosis, an anomaly of development.

COMMENT

The first descriptions of the syndrome were those of Ehlers, of Cohn and of Danlos. The recent rather complete survey of the literature of Ronchese³ makes a further review superfluous. His report included a discussion of 27 cases culled from the literature, with a complete bibliography. To this number were added 3 of his own cases. Smith⁴ stated that the number of complete cases reported was still under 50. In view of this fact, it is singular to note that only 5 cases were reported in the American literature previous to May 1939, by Tobias,² Ronchese,³ Smith,⁴ Brown and Stock⁵ and Rambar.⁶ To these may be added the cases of Weiss,⁷ Tobias⁸ and the Clinic of the Washington School of Medicine.⁹ Numerous other cases of this syndrome reported in the literature were incomplete, the symptoms being confined to hyperelasticity of the skin and abnormal flexibility of the joints.

In cases of dermatolysis the skin is loosely attached to the underlying tissues and has great elasticity and distensibility, similar to that which obtains normally in animals. There are no perceptible changes in the

3. Ronchese, F.: Dermatorrhesis with Dermatochalasis and Arthochalasis, *Am. J. Dis. Child.* **51**:1403 (June) 1936.

4. Smith, C. H.: Dermatorrhesis (Ehlers-Danlos Syndrome), *J. Pediat.* **14**:632, 1939.

5. Brown, A., and Stock, V. F.: Dermatorrhesis: Report of Case, *Am. J. Dis. Child.* **54**:956 (Oct.) 1937.

6. Rambar, A. C.: Ehlers-Danlos Syndrome, *J. Pediat.* **12**:592, 1938.

7. Weiss, R. S.: Danlos' Syndrome, read before the American Academy of Dermatology and Syphilology, St. Louis, Nov. 15, 1938.

8. Tobias, N.: Danlos' Syndrome, Associated with Congenital Lipomatosis, *Arch. Dermat. & Syph.* **40**:135 (July) 1939.

9. Clinics of Washington University School of Medicine: Danlos' Syndrome, *Arch. Dermat. & Syph.* **40**:137 (July) 1939.

texture of the skin, although it feels soft and velvety. The elasticity may be general or confined to certain regions and is especially prominent about the large joints and the face. The subcutaneous fat seems to have disappeared, so that the bony prominences protrude. Another important point is what Danlos described as the vulnerability of the skin, as shown by numerous scars which are scattered over the body. In order for slight trauma to produce such a result, there must be some special vulnerability. Usually the elbows, knees and forehead show these gaping wounds, which heal with wrinkled atrophic scars.

Protuberances in the form of so-called pseudotumors occur at the exposed areas, such as the elbows and knees. They are molluscum-like and have the shape of raisins. They are covered with a glistening, semi-translucent membranous capsule, through which may be seen colors varying from deep red to blue, as in hemangiomas. The formation of the pseudotumors may be explained as follows. When the area is traumatized, the hyperplasia of the elastic tissue causes the wound to retract and form a gaping superficial wound. There is local hemorrhage into the wound, which consists of pockets of blood. When absorption takes place, there remains only a thin, dried-up film, comparable to a fig or raisin.

Recently Weber and Aitkin¹⁰ described a case in which there were numerous cutaneous nodules which were freely movable under the skin and which they called "spherules." The authors expressed the opinion that these lesions were not true lipomas but the result of a deviation from the normal type of the growth of fats, a budlike development of small lobules from the subcutaneous fat. Probably in time they would become minute cysts containing oily substances, with thickened fibrous or even calcerous walls. They considered the lesions a fifth sign of the Ehlers-Danlos syndrome. Coe and Silvers¹¹ presented a case in which the syndrome had been present in four generations and concluded that the condition is inherited as an incomplete syndrome.

The condition in our case fulfils all the requisites of the Ehlers-Danlos syndrome. A complete dermatopathologic picture is given, with the microscopic diagnosis of hyperplastic elastosis, an anomaly of development. The results of chemical examination of the blood were within normal limits and offer no clue to the underlying disease. The results of the chemical examination of the skin are offered as factual observations, their interpretation depending on similar observations on normal skin and on skin in other cases of dermatolysis.

10 Weber, F. P., and Aitkin, J. K. Nature of Subcutaneous Spherules in Some Cases of Ehlers-Danlos Syndrome, *Lancet* **1** 198, 1938.

11 Coe, M., and Silvers, S. H. Ehlers-Danlos Syndrome (Cutis Hyperelastica), *Am J Dis Child* **59** 129 (Jan) 1940.

CONCLUSION

The Ehlers-Danlos syndrome is well defined and constitutes a clinical entity which should be included in the group of congenital dystrophic anomalies. The pathologic findings provide a sound basis for the clinical manifestations. All discussions as to pathogenesis are hypothetical.

225 Eastern Parkway.
555 Prospect Place.

NEUROSYPHILIS AND LATE SYPHILIS OF SKIN, MUCOUS MEMBRANES AND BONES

CLARENCE SHAW, M D

CHATTANOOGA, TENN

One of the tenets held over from the early days of syphilology which is still frequently accepted and taught is the belief that patients with late syphilis of the skin, mucous membrane or bone seldom have neurosyphilis. It is commonly believed that these manifestations of the disease are allergic in origin and influence the immunity reaction so as to protect the neuraxis against involvement by the *Spirochaeta pallida*. Except so-called "precocious tertiary" lesions of the skin, which are on the borderline between those of early and those of late syphilis, and acute syphilis of the bone, which may occur as a phase of early syphilis, these benign tertiary manifestations as a rule appear after the tenth year of the infection. However, as a result of the discovery that a large number of patients with early syphilis show changes in their spinal fluid due to neuraxis involvement, modern syphilologists agree that neurosyphilis is established during the first year of the infection¹. As the infection advances, these changes become more pronounced but not more frequent. In addition, it has been shown that involvement of the nervous system cannot always be detected in early syphilis by the routine examination of the spinal fluid². When one considers these facts, it is difficult to assume that a manifestation which does not appear until the disease is well established in all its phases can be responsible for the suppression or modification of the course of the infection.

The origin of the assumption that benign late syphilis influences the incidence of neurosyphilis is obscure. In all probability it was formulated in the pre-Wassermann era and certainly before the necessity for routine examination of the spinal fluid of all patients with syphilis was apparent. Whatever the origin it has persisted to the present time. Moore³ remarked that it is "comparatively rare for a

From the Public Health Institute, Chicago

1 Keidel, A. Studies in Asymptomatic Neurosyphilis. Apparent Role of Immunity in Genesis of Neurosyphilis, *J A M A* **79** 874 (Sept 9) 1922

2 Chesney, A. M., and Kemp, J. E. Incidence of *Spirochaeta Pallida* in Cerebrospinal Fluid During Early Stage of Syphilis, *J A M A* **83** 1725 (Nov 29) 1924

3 Moore, J. E. Syphilis, in Blumer, G. *The Practitioners Library of Medicine and Surgery*, New York, D Appleton-Century Company, Inc, 1936, vol 10, p 884

patient to suffer from both late mucocutaneous and neurosyphilis, and particularly uncommon for parenchymatous neurosyphilis (tabes or paresis) to be preceded or accompanied by gummatous lesions of skin or bones."

There is no logical reason to believe that lesions of late syphilis of the skin, mucous membrane or bone protect the central nervous system. The absence of neurosyphilis and the presence of benign late syphilis are due to some common factor, perhaps immunity or trophism, but one is not dependent on the other. Therefore, there is no justification for the assumption that the presence of late syphilis of the skin or bone makes routine examination of the cerebrospinal fluid unnecessary.

Previous studies, particularly those of Dercum,⁴ Jeanselme,⁵ Pollitzer,⁶ Bond,⁷ Hoffman⁸ and White,⁹ do not add to the information, since these authors were concerned primarily with the frequency of late cutaneous or osseous lesions in patients with symptomatic and generally advanced neurosyphilis and not with the incidence of neurosyphilis in patients with benign late syphilis.

The following study was undertaken to determine the frequency of the coexistence of syphilis of the central nervous system and late mucocutaneous and osseous syphilis.

The series comprised 165 patients with late syphilis of the skin, mucous membrane and bone who were admitted between 1932 and 1936 to a large venereal disease clinic.¹⁰ The ages ranged from 20 to 69, 9 being Negroes (6 men and 3 women) and the remainder white persons (99 men and 57 women). Selection of subjects was biased only to the point that in each case the diagnosis of the tertiary lesion was unquestionable and the physical examination of the nervous system was adequate. Seventy (42.4 per cent) of the 165 patients had examinations of the spinal fluid before or shortly after the onset of treatment. It is from the cases of this group of 70 patients that conclusions will be drawn.

4. Dercum, F. X.: *The Clinical Forms Presented by Nervous Syphilis*, New York M. J. **98**:745, 1913.

5. Jeanselme, E.: *Elephantiasis syphilitique du membre supérieur*, Bull. Soc. franç. de dermat. et syph. **24**:129, 1913.

6. Pollitzer, S.: *Symposium on Syphilis*, Post Graduate **28**:729, 1913.

7. Bond, E. D.: Personal communication to C. J. White.

8. Hoffman, J. A.: *A Report of the Patients Discharged from the John G. Kerr Hospital for Insane During 1912*, China M. J. **27**:369, 1913; *Insanity in China*, Boston M. & S. J. **170**:572, 1914.

9. White, C. J.: *A Statistical Study of Syphilis: The Relation of Its Symptoms to Subsequent Tabes Dorsalis or General Paresis*, J. A. M. A. **63**:459 (Aug. 8) 1914.

10. Public Health Institute, Chicago.

This group can be compared with a control group of cases taken from the files over approximately the same time interval¹¹ In this control group of over 700 cases, the incidence of neurosyphilis was established by spinal fluid examinations and represents the incidence of neuraxis involvement in the clinic as a whole

RESULTS

Fifteen patients (12 men and 3 women), comprising 21.4 per cent of the 70 who had complete examinations of the nervous system (including examinations of the spinal fluid), had positive reactions of the spinal fluid Seven, or 10 per cent, of the 70 patients had asymptomatic neurosyphilis In those patients classified as having asymptomatic neurosyphilis, physical examination revealed at the most only suggestive evidence of neuraxis involvement, such as slight irregularity of the pupils, sluggish reaction to light and hypoactive or hyperactive deep reflexes In no instance would it have been possible to make a positive diagnosis of involvement of the nervous system from the history or physical examination without the positive result of the spinal fluid examination

Approximately 40 per cent of the 700 control patients had serologic evidence of neurosyphilis Twenty-five per cent of this group had asymptomatic neurosyphilis¹²

COMMENT

Many modern investigators have contributed large series of cases as evidence against the theory of an antagonism between late mucocutaneous or osseous syphilis and neurosyphilis Arzt and Fuhs¹³ reported a series of 350 cases of tertiary syphilis of the skin and mucous membrane, in 29 per cent of which the spinal fluid gave a positive reaction These authors reported an additional 300 similar cases in which 32 per cent had spinal fluid with a positive reaction, but only 10 per cent had clinical involvement of the nervous system Hval¹⁴ reported 95 cases, in 70 of which there were examinations of the spinal fluid Of

11 Kemp, J. E., and Menninger, W. C. The Influence of Pregnancy upon the Course of Syphilis, *Brit. J. Ven. Dis.* **12** 206, 1936

12 Menninger, W. C., and Kemp, J. E. The Incidence of the Clinical Types of Neurosyphilis in Males, Pregnant and Non-Pregnant Females, *J. Nerv. & Ment. Dis.* **83** 275, 1936

13 Arzt, L., and Fuhs, H. Liquor- und klinische Nervenveränderungen bei tertiärer Haut- (Schleimhaut-) Lues und ihre Beurteilung, hinsichtlich Prognose und Therapie, *Arch. f. Dermat. u. Syph.* **163** 164, 1931, Liquor und tertiäre Haut- (Schleimhaut-) Lues, *ibid.* **166** 427, 1932, Manifeste Neuroloues (Lues cerebrospinalis, Tabes, progressive Paralyse) bei Tertiäre Haut- (Schleimhaut-) Lues, *ibid.* **166** 234, 1932

14 Hval, E. Condition of Cerebrospinal Fluid in Gummatous Syphilis, *Acta dermat.-venereol.* **13** 643, 1932

these, in 14, or 20 per cent, the spinal fluid showed pathologic changes; without elaborating, he stated that in 6 of the 14 the changes were slight. O'Leary and Rogin,¹⁵ examining the records of 100 cases of tertiary syphilids, found positive reactions in the spinal fluid in 20 cases, in 10 of which there were clinical signs of involvement of the nervous system. In addition, 4 patients were observed with signs of syphilis of the central nervous system but with negative reactions of the spinal fluid. In the majority of their patients with clinical neurosyphilis the disease was of the tabetic type.

Konrad¹⁶ reported syphilis of the central nervous system in 19 per cent of 300 cases, and Grschebin,¹⁷ in 13 per cent of 300 cases.

Merenlender,¹⁸ in his review of the literature to 1932, was able to collect 352 authentic and proved cases of coexisting syphilis of the central nervous system and late syphilis of the skin or bones.

The accompanying table allows a comparison of figures presented by various authors. All forms of neurosyphilis occurred in from 13

*Incidence of Neurosyphilis in Cases of Late Syphilis of the Skin,
Mucous Membranes and Bones*

Authors	Total Number of Cases	Per Cent of Cases of Syphilis of the Central Nervous System
Arzt and Fuhs.....	300	32.0
Arzt and Fuhs.....	350	29.0
Hyal.....	95	20.0
O'Leary and Rogin.....	100	24.0
Konrad.....	300	19.0
Grschebin.....	300	13.0
Shaw.....	70	21.4
Total.....	1,515	22.6

to 32 per cent of patients with mucocutaneous or osseous tertiary syphilis.

The high incidence of asymptomatic neurosyphilis in this series is of particular importance. It would have been highly desirable to know how many more such cases would have been discovered had it been possible to examine the spinal fluid of the entire group of patients with benign late syphilis.

The fact that almost twice the number of patients in the control group as in the experimental group had neurosyphilis (40.4 per cent as against 21.4 per cent) indicates that there may be a difference in

15. O'Leary, P. A., and Rogin, J.: Late Cutaneous Syphilis, *Am. J. Syph.* **16**:98, 1932.

16. Konrad, J.: Lues gummosa und Liquorveränderungen, *Arch. f. Dermat. u. Syph.* **162**:102, 1930.

17. Grschebin, S.: Beitrag zur Frage nach der Entstehung der Neurolues, *Arch. f. Dermat. u. Syph.* **159**:284, 1930.

18. Merenlender, J.: Gibt es einen Antagonismus zwischen Haut- und Metalues? *Zentralbl. f. Haut- u. Geschlechtskr.* **43**:1, 1932.

immunity in the patients who have benign late syphilis. If this phenomenon is due to a difference in immunity, it must be considered that the allergic state is established early in the course of the disease, *i e*, before involvement of the nervous system by the spirochete occurs. This difference in the defensive powers of the body, rather than the allergic manifestations themselves, accounts for the partial protection of the neuraxis. This protection is at best only partially efficient, and with an incidence of asymptomatic neurosyphilis that is equal to 1 of 5, the necessity of performing routine lumbar punctures in all cases of benign late syphilis is obvious.

SUMMARY AND CONCLUSIONS

Fifteen (21.4 per cent) of 70 patients who had late mucocutaneous or osseous syphilis and whose spinal fluid was examined had neuraxis involvement. Seven (46.7 per cent) of the 15 had symptomatic neurosyphilis, and 8 (53.3 per cent) had asymptomatic neurosyphilis.

Approximately 40 per cent of a control group of over 700 patients representative of the clinic population as a whole had neurosyphilis.

From the material gathered from the literature and from the present analysis, it may be conservatively stated that from 1 of 10 to 1 of 3 patients with late mucocutaneous or osseous syphilis have syphilis of the central nervous system.

Examination of the spinal fluid is definitely indicated for all patients with benign lesions of late syphilis.

1021 Provident Building

COMPARISON OF OLD TUBERCULIN (KOCH) AND MODIFIED TUBERCULIN (MELLON AND BEINHAUER)

CUTANEOUS REACTIONS IN PERSONS WITH HYPERERGIC AND
WITH ANERGIC TUBERCULODERMS

LUDWIG SCHWARZSCHILD, M.D.

NEW YORK

In the opinion of most students the majority of sarcoids are considered to be a form of tuberculosis. Most patients with sarcoids usually fail to react to Mantoux tests with tuberculin even in high concentrations. This lack of reaction to tuberculin in the usual dilutions is sometimes a helpful diagnostic criterion in the diagnosis of sarcoid. J. Jadassohn, Martenstein, W. Jadassohn and many others, including some American authors,¹ explained this lack of reaction as a positive specific tuberculin anergy connected with the presence of anticutins in the blood serum and in the tissues of patients with sarcoids.

A new and different explanation for the pathogenesis of sarcoids and for the negative reaction to tuberculin in patients with these diseases was recently advanced by Mellon and Beinhauer.² They reported that they were able to recover from one Negro patient with noncaseating tuberculosis a "partially acid-fast actinomycotic organism"^{2a} and from another patient a "diphtheroid bacillus containing strongly acid-fast granules."^{2b} They considered both these types to be an integral part in the life cycle of the tubercle bacillus and to be dissociants of Koch's bacillus.

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University.

Cases 4 and 5 were included in this series with the permission of Dr. Paul Gross.

1. Sulzberger, M. B.: *Sarcoid of Boeck (Benign Miliary Lupoid) and Tuberculin Anergy*, *Am. Rev. Tuberc.* **28**:734, 1933. Sulzberger, M. B., and Wise, F.: *Tuberculin: Newer Dermatological Considerations and Reasons for Its More General Use in Diagnosis*, *M. Clin. North America* **14**:1555, 1931. Sulzberger, M. B., and Goodman, J.: *Tuberculoderms*, *ibid.* **20**:995, 1936.

2. Mellon, R. R., and Beinhauer, L. G.: (a) *The Pathogenesis of Non-caseating Tuberculosis of the Skin and Lymph Glands*, *Arch. Dermat. & Syph.* **36**:515 (Sept.) 1937; (b) *Pathogenesis of Noncaseating Epithelioid Tuberculosis of Hypoderm and Lymph Glands*, *ibid.* **37**:451 (March) 1938.

TABLE 1—*Comparison of Reactions to Various Concentrations of Old*

Num ber	Race	Clinical Diagnosis	Histologic Diagnosis	1 1,000,000			1 100,000			1 10,000		
				Old Tuber- culin (Koch)	Modified Tuberculin		Old Tuber- culin (Koch)	Modified Tuberculin		Old Tuber- culin (Koch)	Modified Tuberculin	
					Hu- man	Avian		Hu- man	Avian		Hu- man	Avian
1	Negro	Sarcoid Boeck	Sarcoid Boeck	—	—	—	—	—	—	—	—	—
2	White	Sarcoid Boeck	Sarcoid Boeck	—	—	—	—	—	—	—	—	—
3	White	Sarcoid Boeck	Sarcoid Boeck simulating lupus vulgaris	—	—	—	—	—	—	±	—	—
4	Negro	Sarcoidosis	Sarcoid Boeck	—	—	—	—	—	—	±	—	±
5	Negro	Sarcoid Boeck	Sarcoid Boeck	—	—	—	—	—	—	+	—	—
6	White	Sarcoid?		—	—	—	—	—	—	—	—	—

TABLE 2—*Comparison of Reactions to Various Concentrations of Old
Tuberculoderms*

Num ber	Race	Clinical Diagnosis	Histologic Diagnosis	1 1,000,000			1 100,000			1 10 000		
				Old Tuber- culin (Koch)	Modified Tuberculin		Old Tuber- culin (Koch)	Modified Tuberculin		Old Tuber- culin (Koch)	Modified Tuberculin	
					Hu- man	Avian		Hu- man	Avian		Hu- man	Avian
7	White	Lupus vulgaris		+	(+)	±	+(+)	+	—	+	(+)	+
8	White	Lupus vulgaris	Lupus vulgaris	+	—	—	+	—	—	+	—	+
9	White	Rosacea like tuberculid		—	(±)	—	—	—	—	±	—	—
10	White	Rosacea like tuberculid	Rosacea like tuberculid	—	—	—	—	—	—	—	—	+
11	White	Rosacea like tuberculid		—	—	—	+	—	—	++	—	—
12	White	Rosacea like tuberculid	Folliculitis	—	—	—	(±)	—	—	(±)	—	—
13	White	Lewandowsky? Rosacea?		—	—	—	—	—	—	+	—	—
14	White	Papulonecrotic tuberculid		—	—	—	—	—	—	—	—	—
15	White	Erythema indu- ratum (Bazin)		—	—	—	—	—	—	—	—	—
16	White	Granuloma annulare? Lupus erythema- tosis?		(±)	±	—	+	—	—	+	+	±

Tuberculin (Koch) and to Two Modified Tuberculins in Patients with Sarcoid

<i>(Koch) and to Two Modified Tuberculin in Patients with Sarcoid</i>																			
1:5,000				1:1,000				1:500				1:100				1:10			
Old Tuberculin (Koch)		Modified Tuberculin		Old Tuberculin (Koch)		Modified Tuberculin		Old Tuberculin (Koch)		Modified Tuberculin		Old Tuberculin (Koch)		Modified Tuberculin		Old Tuberculin (Koch)		Modified Tuberculin	
Human	Avian	Human	Avian	Human	Avian	Human	Avian	Human	Avian	Human	Avian	Human	Avian	Human	Avian	Human	Avian	Human	Avian
-	-	-	+	-	-	+++	(+)	-	-	+++	(+)	-	-	+++	+++	-	-	±	(+)
±	-	-	±	-	-	-	+++	-	-	-	++	(+)	-	-	+++	-	-	-	-
+	-	-	+	-	-	-	+++	-	-	++	(+)	-	-	++	+++	-	-	+	-
+	-	-	+++	-	-	-	+++	-	-	-	++:	-	-	-	++++	-	-	-	-
+++	-	-	++	?	-	++	(±)	-	-	++:	+++	-	-	-	+++	-	-	-	-
-	-	-	-	-	-	+	-	-	-	++:	+++	-	-	-	+++	-	-	-	-
										++:	+++	-	-	-	+++	-	-	±	-
										++:	+++	-	-	-	+++	-	-	±	-

*Tuberculin (Koch) and to Two Modified Tuberculins in Patients with
Other Than Sarcoid*

Old Tuberculin (Koch)	1:5,000		1:1,000		1:500		1:100		1:10	
	Modified Tuberculin		Modified Tuberculin		Modified Tuberculin		Modified Tuberculin		Modified Tuberculin	
	Human	Avian	Human	Avian	Human	Avian	Human	Avian	Human	Avian
	Old Tuberculin (Koch)	Old Tuberculin (Koch)	Old Tuberculin (Koch)	Old Tuberculin (Koch)	Old Tuberculin (Koch)	Old Tuberculin (Koch)	Old Tuberculin (Koch)	Old Tuberculin (Koch)	Old Tuberculin (Koch)	Old Tuberculin (Koch)
..
++	-	-
+	-	-
(+)	-	-	++	-	++	±
+++	-	-	+++	-	+++	-	+++	+++	+++	+++
+	-	-	+++ (±)	+++	+++ (±)	-	+++	+++	+++	+++
(+)	-	-	+++ (±)	+++	+++ (±)	-	+++	+++	+++	+++
-	-	-	+++	+++	+++	-	+++	+++	+++	+++
-	-	-	+++	+++	+++	-	+++	+++	+++	+++
+++	-	-	+++	+++	+++	-	+++	+++	+++	+++

Mellon and Beinbauer concluded from these observations that the infection in sarcoid is caused by the critical rough form of the tubercle bacillus, which is avirulent or of lowered virulence, and that later these micro-organisms become dissociated into one of the non-acid-fast culture phases. On this basis they explained that patients with sarcoids often show less than normal reaction to old tuberculin, which is an extract of the acid-fast forms. This hypothesis is supported by the fact that Mellon and Beinbauer found that, although their patients gave negative reactions to intradermal tests with old tuberculin (Koch) in dilution of 1:1,000, they gave positive reactions to cutaneous tests with tuberculin prepared from a critical rough form of the bacillus.

In order to study this problem further, Dr. Marion B. Sulzberger suggested that I investigate a number of cases of sarcoids and of other unequivocally tuberculous cutaneous lesions simultaneously with old tuberculin (Koch) and with two specimens of freshly prepared tuberculin (Mellon and Beinbauer) made from critical rough forms of the tubercle bacillus (the latter were placed at the disposal of Dr. Sulzberger by Dr. Beinbauer). These two tuberculins represent strains from a human and an avian critical rough form.

At the outset I tested a guinea-pig that previously had been sensitized by infection with BCG and was found to be strongly hypersensitive to cutaneous tests with old tuberculin. I injected intracutaneously into this animal 0.1 cc. of old tuberculin (Koch) of a concentration of 1:900. This caused a strongly positive reaction at the site of the injection after forty-eight and seventy-two hours. The modified tuberculins made from the human and from the avian critical rough forms of the tubercle bacillus were injected into this animal in concentrations of 1:1,000 and 1:100. The reactions to these two tuberculins were entirely negative.

I then compared the reactions to old tuberculin and to these two modified tuberculins in 6 cases of sarcoid. Three of the patients were Negroes, and 3 were white. In 5 of the 6 patients the clinical diagnoses were verified by histologic examination.

As is to be seen from table 1, and contrary to the findings of Mellon and Beinbauer, none of our patients with sarcoid reacted to either one of the two modified tuberculins in dilutions of 1:1,000,000, 1:100,000, 1:10,000, 1:5,000 or 1:1,000 (the plus-minus reaction to a 1:10,000 dilution in case 4 was most probably a "traumatic" reaction). Even with the higher concentrations, i. e., 1:500, 1:100 and 1:10, I could elicit no definite reaction with the two modified tuberculins but only mild reactions, plus-minus or 1 plus, in 4 patients. Furthermore, there was no parallelism in the reactions to the human and the avian tuberculins. On the other hand, I did get reactions in several cases to old tuberculin in dilutions of 1:10,000 and more conspicuous reactions with the higher concentrations.

In addition to these cases of sarcoid, I tested 10 patients with other tuberculoderms. As seen in table 2, the reactions in those cases were rather irregular. Sometimes the higher concentrations of the Mellon and Beinhauer tuberculins produced weaker reactions than did the more diluted ones (paradox reactions). A comparison of the two modified tuberculins showed no correspondence; i. e., I was not able to confirm with my tests the assertion that the tuberculin made from a critical rough avian strain is not distinguishable from that derived from a critical human strain. On the other hand, I noticed in some patients equal reactions to old tuberculin and to one or both of the modified tuberculins.

SUMMARY

In 6 cases of sarcoid of Boeck I was not able to elicit reactions with two special tuberculins made, respectively, from critical rough avian and critical rough human strains of the tubercle bacillus, in concentrations of 1:1,000 or even in higher concentrations. This finding stands in apparent contradiction to the reports of Mellon and Beinhauer.

In 10 cases of various other tuberculoderms there was no parallelism between the reactions produced by these two modified tuberculins.

In some cases of tuberculoderms equal degrees of reactions to old tuberculin and to one or both of the modified tuberculins were noted, and in other cases there was no correspondence between reactions to old tuberculin and those to the modified tuberculins.

My findings do not support the theory that sarcoids are due to a critical rough form (nonacid-fast dissociant) of a tubercle bacillus.

514 West End Avenue.

EFFECT OF ULTRAVIOLET RADIATION ON ROENTGEN RAYS

DO ULTRAVIOLET RAYS HAVE A DELETERIOUS EFFECT ON ROENTGEN
RAYS WHEN APPLIED TO THE SKIN?

FRANCIS A ELLIS, M D

BALTIMORE

AND

HAYDEN KIRBY-SMITH, M D

WASHINGTON, D C

Cutaneous Irritants Have a Detrimental Effect on Roentgen Ray Therapy—The question is still unsettled as to whether ultraviolet radiation from natural or artificial sources has a deleterious or complementary effect on skin which has been exposed to it in conjunction with roentgen rays MacKee¹ praised the judicious use of roentgen therapy in the treatment of acne but advised against the concomitant use of stimulating remedies, such as sulfur and mercury ointments, sulfur lotions, resorcinol lotions and other similar mild cutaneous irritants He stated that exposure to erythema doses of ultraviolet rays and excessive sunlight is not advisable while the patient is receiving roentgen ray treatments Many dermatologists questioned by one of us (F A E) have concurred in MacKee's contentions, and they have cited cases in which roentgen ray dermatitis developed after roentgen therapy in doses which they considered to be suberythema, plus exposure to sunlight and/or irritating topical applications

Lambadaridis² stated that after a single exposure to roentgen rays the patient must be protected for the next six months from wounds, infections and especially exposure to sunlight and other forms of ultraviolet radiation He stated that some children were given, for tinea of the scalp, a correct (?) epilating dose of roentgen rays, which caused permanent alopecia He was of the opinion that the children may have received an actinic dermatitis from the intense sun rays on the coast of Greece, and this plus the roentgen treatment had destroyed the hair follicles

1 MacKee, G M X-Rays and Radium in the Treatment of Diseases of the Skin, ed 3, Philadelphia, Lea & Febiger, 1938, p 406 MacKee, G M, and Andrews, G C The Ultraviolet Ray as a Prophylactic Against Radiodermatitis, J A M A 85:1715 (Nov 28) 1925

2 Lambadaridis, A Biologische Effekt bei kombinierter Einwirkung von Rontgen- und Sonnenstrahlen, Radiologica 2 206, 1938

Ultraviolet Radiation Has a Favorable Effect on Roentgen Ray Therapy.—Sampson³ considered roentgen and ultraviolet rays as physiologic complements in therapeutics. He stated that the stronger the actinic ray reaction, the more stimulating it is to growth of hair and that one or two "good erythemas" due to ultraviolet radiation are usually sufficient to arrest alopecia caused by roentgen rays. He stated the opinion that after ultraviolet ray dermatitis the falling out of hair is checked, that there is a stimulation of the hair follicle, which results in an extra rapid growth of normal hair, that lanugo hair often becomes more abundant and increases in size and, in some cases, that even the pigment returns. He demonstrated by experiments on patients that previous exposure to actinic rays increased the tolerance to subsequent erythema and higher doses of roentgen rays.

Traub⁴ gave ultraviolet ray treatment to patients at the end of courses of roentgen therapy in an effort to efface the scarring and to preclude future untoward roentgen ray sequelae. The treatments were given in sufficient amounts to cause second degree erythema and thorough peeling of the skin. Traub also used the two forms of therapy alternately and stated the opinion that this resulted in more rapid improvement, without the risk of roentgen ray dermatitis.

Rulison⁵ gave a course of ultraviolet ray treatments with a Kromayer lamp to an area of skin which had been exposed to "four and a half skin units" of unfiltered roentgen rays. A filter had been omitted by mistake. The ultraviolet radiation was given immediately after the roentgen ray treatment. He stated that the treatments with the lamp prevented a severe reaction. However, since the radiation was given through a 2.5 cm. portal, a severe reaction following the exposure to the dose given would not necessarily be expected.

"Roentgen Ray Skin" Due to Natural and Artificial Lights.—It is well known that actinic rays will cause "roentgen-ray-like" changes in the skin, consisting of atrophy of the epidermis, abnormal pigmentation or hyperpigmentation, dilated capillaries, senile elastosis, keratosis and even malignant degeneration. This type of change occurs at an early age in patients with xeroderma pigmentosum and later in persons subjected to excessive exposure to the elements, for example, seamen and farmers.

3. Sampson, C. M.: Ultraviolet and X-Ray as Physiologic Complements in Therapeutics: A Newly Established Clinical Treatment, *Am. J. Roentgenol.* 9:570, 1922.

4. Traub, E. F.: The Treatment of Acne by the Combined Use of the X-Ray and the Mercury Quartz Light, *M. J. & Rec.* 122:90, 1925.

5. Rulison, R. H.: Prophylaxis of Roentgen-Ray Overdosage, *J. A. M. A.* 83:1505 (Nov. 8) 1924.

Schuermann⁶ reported 2 cases of "roentgen ray skin" in patients who had never received any roentgen rays. One patient had received radiation therapy with a Finsen lamp over a long period for lupus vulgaris. The other patient was treated with radiation from a quartz mercury vapor lamp for many years for eczema. No porphyrinuria was found.

The Combined Use of Roentgen Rays and External Irritants, Including Light Rays—Simpson⁷ in 1931 reported a technic for treating acne which consisted essentially of giving a third of an erythema dose⁸ of roentgen rays every ten days and an erythema dose of ultraviolet rays every ten days. Thus the patient was treated every five days with the alternate modes of therapy. In 1939 we examined 11 patients who had received ten to sixteen (average, thirteen and a half) one-third erythema doses of roentgen rays and during the same period of time had also received four to twenty-one (average, ten and a half) erythema doses of ultraviolet rays. All of the patients also applied to the treated areas the following: 7.5 Gm each of prepared chalk, glycerin, zinc sulfate, sulfured potash and precipitated sulfur (6.25%) and orange flower water to make 120 cc. Directions: Lotion. Apply at night.

This was considered to be a two ply (6.25 per cent) acne lotion, and the active ingredients were increased up to six ply (20 per cent) as the tolerance of the patient's skin permitted. The chalk was omitted from the stronger preparations.

When treatment was started the ages of the patients varied from 14 to 36 (average, 26). The time from the termination of treatment to the reexamination was from three to eight (average, four and one-half) years. Nine patients had had subsequent roentgen and actinic ray therapy after the original course of treatments. None of the patients showed any evidence of roentgen ray dermatitis, in fact, in half of the patients there was an excess of oil on their faces, and in most of the patients some acne lesions still developed. In the 2 youngest patients there were enough lesions to be objectionable. This routine of therapy has been replaced in the past few years by a technic of giving approximately 70 r weekly. We have continued to use the modified white lotion concurrently, without any ill effects.

COMMENT

In our opinion the roentgen therapy has simply an additional action on actinic effect on the skin, for instance, if "R" represents the

6 Schuermann, H. "Röntgenhaut" ohne Röntgenbestrahlung, *Dermat Wchnschr* 105 945, 1937.

7 Simpson, C. A. Observations in Five Hundred Cases of Acne, Treated with 2,432 Exposures of X-Ray, *Virginia M. Monthly* 58 535, 1931.

8 Dosage was based on the physical formula as described by MacKee

$$\frac{3 \text{ ma.} \times (90\text{KV})^2 \times 3 \text{ min}}{(10 \text{ in})^2} = 1 \text{ erythema dose}$$

permanent or late roentgen ray effect and "A" the permanent actinic change on the skin, then the total late changes will equal "R" plus "A." When "R" and "A" are given simultaneously, alternately or later, neither exerts a beneficial or deleterious action on the other but only a summation of one plus the other.

What is the explanation for the difference of opinion as expressed in the literature? MacKee's conclusions were based on data in the era before the roentgen unit was defined and apparently when dosage was inaccurate. Lambadaridis' discussion seems fairly convincing, but his dosage of radiation was not stated, nor were his standards of units expressed. His statement that the patient who receives a single roentgen ray exposure must be protected for six months from all external irritants does not seem to be justifiable. We believe that Sampson apparently has overestimated the value of actinic rays. Every dermatologist will no doubt agree that ultraviolet ray therapy hardly possesses all the properties Sampson claims for it, such as stopping the loss of hair and promoting the change of lanugo hair to the terminal type. Traub⁹ stated that after fifteen years of giving roentgen ray therapy in conjunction with ultraviolet ray treatment he has not seen any harmful effects in the skin. He advised against giving both types of therapy on the same day, as he stated the opinion that this will definitely increase the reaction to both agents.

SUMMARY

It is our opinion that the former lack of adequate accurate measurements of dosage, mistakes in technic and overdosage are the main causes for roentgen ray sequelae and not a concomitant actinic dermatitis or/and a dermatitis due to external irritants.

The late cutaneous changes due to the combined application of roentgen rays and actinic rays are usually a summation of one plus the other, and the combined use of the two modes of therapy does not accentuate the effect of either agent.

The mechanical formula of MacKee is adequate for varying dosage once a standard in roentgens or erythema doses is determined, but there is a decided variation in the output of tubes with the same voltage, milliamperes, distance and time.

This combined method of therapy should be repeated with all factors controlled by modern methods and standards of measuring roentgen ray dosage. For over two years we have used strong sulfur lotions in conjunction with accurately measured roentgen therapy in the treatment of acne, without any evidence of roentgen ray sequelae.

8 East Madison Street, Baltimore.

1610 Twentieth Street Northwest, Washington, D. C.

9. Traub, E. F.: Personal communication to the authors.

THE "SPIRITUAL" VALUE OF SYPHILIS

THEODORE SCHROEDER, M D

COS COB, CONN

Thirty years ago claims for the spiritual and moral value of syphilis were upheld by many "good people" In 1911 in the state of New York the passage of a law was almost secured to penalize persons responsible for announcements that venereal diseases are curable It was argued that such information would help to make vice safe and would therefore promote immorality Much of that attitude still exists and is the basis for much opposition to all education for venereal prophylaxis

A friend, who is much interested in such education, restated to me all the objections to such education which had come to his notice He knew of my successful opposition to the passage of the bill referred to, and he also knew of my amoral attitude to every aspect of sex He asked me to answer the objections which he had relayed to me Herein I give his version of the objector's attitude and my reply No argument will be made There will be only the dogmatic statements of a modern amoral scientist in reply to the equally dogmatic contrary assertions of moralists

1 "Venereal prophylaxis is immoral"

The answer that any one makes to that assertion will depend on several factors If the answer is determined by the compulsions of a "split personality," it will be either a positive and emphatic "yes" or "no" If the answer is made by a well unified personality, that is, by one who at the same time is well informed about the history and psychology of morals, then the question will receive no direct answer The completely scientific attitude toward sex and everything human is thoroughly amoral From this point of view all moral judgments and values, whether old or new, are the symptomatic product of a so-called "split personality" or of the imitation of such That is to say, all such moral judgments and values are a consequence of an inner conflict of impulses, with varying degrees of approach to a pathologic intensity This attitude has its beginning in the avoidable delusional fears and artificial lures that all moral training tends to implant in infancy and childhood

2 "Venereal prophylaxis encourages promiscuity"

That seems important to all psychoneurotic moralists who rationalize their emotional indigestion in terms of ascetic morality Some who believe in "new morals for old" blindly assume this to be beneficial Such moralists are usually obsessed with the idea that sexual relations,

under any of their "fifty-seven varieties" of conditions, must be moral or immoral and therefore must be harmful or beneficial to the parties concerned, to their everlasting soul and to society. For ascetics, that "spiritual" injury is usually thought of as being remote and indirect, inflicted by means of damage to a hypothetical soul. Those who are more healthy minded, psychologically more mature and intellectually better informed will assume that promiscuity in itself is neither injurious nor beneficial to the person or to the race. Such conclusions are to be made according to the actual or probable physical or mental consequences, which are the varying product of numerous associated conditions. These consequences are judged according to the operation of known "natural laws" and in the light of the alternatives. All is relative. Promiscuity which spreads venereal disease is less desirable than that which does not. Promiscuity which is so conditioned that it does not either promote venereal disease or intensify the conflicting impulses (like those of a dual personality) is preferable to a sanctified monogamic relation which produces infected offspring or spreads syphilis by non-sexual methods and at the same time increases psychologic morbidity. Sexual relations under identical physical conditions may have the effect of retarding or of accelerating the psychologic maturing of one or both parties concerned or of promoting a psychologic regression. These results will be determined by the psychologic preparedness (degree of objectivity) of the parties concerned and by the environmental factors that are coordinated with that predisposition. It is according to these realistic (psychologic and physical) consequences of sexual relations that the amoralist passes his judgment on the relative merits of differing lines of conduct. For him nothing is approved or disapproved by means of an abstraction from all the causes and consequences of the whole situation.

3. "Venereal prophylaxis will encourage men and women who now abstain from sexual relations for fear of venereal disease to extramarital sexual indulgence."

The fear of syphilis, purgatory or hell fire will not prevent the functioning of the sex glands. The only question is: How do they function? What are the consequences? Under great fear, it is possible to exclude all the physical facts of sex from consciousness and to delude one's self into thinking that the psychologic consequences are unrelated to physical sexual experience. Is the functioning of the glands autogenic or with a physical external stimulation? Is it physiologic or psychologic autoerotism, or homosexual or heterosexual indulgence? Men and women should be fully informed of the physical and psychologic consequences that flow from the functioning of their sexual glands. They should be taught to respect the "natural laws" of their own organism in its psycho-

logic as well as its physiologic aspects. It is more important that they adjust their lives and emotions to "natural laws" than to the moral superstitions of their neighbors. Emotionally toned artificial fear, whether of hell fire, venereal disease or moral condemnation, is an injury to mental health and is reprehensible to the same degree as the intensity of such fear. This is an injury to the person and to society, because the resulting emotional imbalance promotes antisocial behavior, even criminal acts and insanity. The responsibility for all such consequences and most of the changes observed in criminal psychology rest with the moralists who instil such artificial fears and deluding hopes and a corresponding disrespect for "natural law."

4 "Venereal prophylaxis is in bad taste and is unesthetic. Every time lovers embrace and use a prophylactic they will think in terms of disease and not of pleasure."

This statement will be true only if the persons have first been made psychoneurotically fearful by pathologic moralists, their following of moralists for revenue and the ignorant imitators of these. Unmarried lovers will find themselves further dissatisfied if, through the influence of the erudite infantilism of educators and moralists, they concentrate only on the pleasures of the moment. If, however, a greater degree of healthy mindedness and psychologic maturity have been allowed to develop, then the lovers will give relatively little attention to the pleasures of the moment and will concern themselves more with the remote consequences which their present sexual activities will produce on their whole organism, both the physical and the psychologic effects. The mental infants in mature bodies, like their mentors the pathologic moralists, will not understand what that means. If they prefer their momentary esthetics to freedom from lifelong emotional disorders and venereal disease, then I suppose they can have it, since no one can force them to use prophylactics or grow up mentally.

5 "Venereal prophylaxis is unnecessary. Only the stupid and ignorant and those who deserve to be infected ever catch gonorrhea or syphilis."

This statement is wholly untrue. Under the influence of temporary sexual suppression, so great a passion develops that it compels one to ignore whatever "intelligence" one may have had on the subject. Furthermore, if syphilis became more prevalent, more people would take it for granted and become more careless, and there would be an ever increasing number "innocently" infected, through drinking utensils, towels and toilet facilities. It is this type of infection which justifies the appellation "social disease."

6 "Venereal prophylaxis is against the economic interest of physicians. Syphilis and gonorrhea are about the only diseases left from which the general practitioner can make a little money."

That statement is not true, but it may be a matter of considerable influence with some doctors. Those who are thus influenced are, of course, the ones who are of least credit to their profession. Those who frankly avow such a position will be few. Physicians who wish to promote venereal disease in others in order to promote their own welfare should be removed from the profession. Many who are motivated by such considerations will conceal their real aims by adopting other less honest arguments, such as are here being answered. In such cases, their choice of position and of argument will usually be dictated by some psychoneurotic compulsion. They should seek a mental cure rather than an answer to their arguments.

7. "Venereal prophylaxis is against the teachings of the church. The wages of sin is death. As you sow so shall you reap. Prophylaxis permits men and women to escape the penalty of sin."

This is the same old, old objection that at some time has been made to every advance in every branch of secular education, to the methods of medical healing, to the alleviation of pain and to all prophylaxis and hygiene in the beginning. Vice must not be made safe by making child bearing painless or by making it possible to have sexual intercourse without sorrow. At sometime or other all diseases have been regarded as God's punishment for the disobedience of His commands and the failure to support His clergy. Now, as in every past historical period, healthy-minded progressive people have had to combat this old fundamentalist and ascetic morality. Always the implication is that one can only merit heaven by making earthly life a vale of tears. For further answer, see the preliminary remarks and my answer to the first objection.

8. "Venereal prophylaxis is a poor policy for a city, state or federal health department to adopt, because if taxpayers and lawmakers who appropriate the money for this type of education understand that it will give foolish people protection and will encourage 'immorality' and promiscuity, they will not make large appropriations."

That is exactly the same argument that was made against every basic advance in the physical sciences, the establishing of secular schools and state universities and all laws for sanitation. All this interfered with some fundamentalist's conception of morals. It did result in smaller appropriations and will do so again, but these were better than none at all. The larger contributions and appropriations come with a later appreciation of the social benefits. There are many fundamentalists who still have that attitude toward secular education; I have heard them called "funnymentalists." With venereal prophylaxis it is as with other education. Even the average man will eventually discover that venereal disease is to be regarded as other contagious diseases and that it is cheaper and better to prevent disease than to cure it, even though the disease is a venereal one.

9 "Prophylaxis and birth control will (1) remove all barriers and restraints on the impulses that make for 'free love,' polygamy and polyandry, causing men and women to be debauched and think of nothing but sex and lasciviousness and (2) cause civilization and decency to be lost "

Let me counter the second proposition first Only a sexual maniac with a morbid feeling of guilt over his own sexual peccadillos could invent the theory that civilization and any particular form of sexual expression are identical It is indeed true that for the better mental hygiene, a new attitude toward and a new understanding of sexual psychology are necessary In that sense sex is important However, the preservation and glorification of the puritanic symptoms of the general emotional imbalance are not the best but the worst part of civilization

If a knowledge of venereal prophylaxis and birth control does result in any sudden outbreak of sexual excesses, it will not be due to that education On the contrary, it will only mean the release of impulses that were already there and suppressed with morbid intensity These were made morbid by puritanic leaders, through their effort to control the sexual life of children by means of artificial fears and delusional hopes, instead of unemotional realistic education for understanding and respecting only "natural laws" even as to sex The knowledge of birth control and venereal prophylaxis does not create that morbidity It was preexistent Only its normal heterosexual expression was inhibited by artificial fear It may be true that this new knowledge in some instances will increase the more normal indulgence at the expense of perversion It will not increase lasciviousness but in time is apt to reduce it I am not so much concerned with the existing abnormal type as I am with the emotional health of the coming generation The giving of free, adequate and accurate information about even the psychology of sex, under circumstances which increase their respect for "natural laws" (including those of psychosexual maturing and psychosocial evolution), can be made a great aid to mental hygiene and so reduce the antisocial types now produced by morbid moralists

FREQUENCY OF CERTAIN DERMATOSES IN HIGH SCHOOL GIRLS

REPORT ON 4,700 GIRLS

IDA J. MINTZER, M.D.

JAMAICA, N. Y.

Comparatively little attention has been given in medical examinations of school children to the common dermatoses, and a survey of the literature reveals no statistics on this subject for girls of high school age. The psychologic importance of even trivial cutaneous blemishes to adolescent girls, not to mention the possible debilitating effect of some of these minor dermatoses on the general health, should make them of greater interest to the dermatologist and to the general practitioner than their intrinsic importance might otherwise seem to warrant.

The girls examined in this series were between the ages of 13 and 18. Acne, as might be expected, was by far the most prevalent dermatosis, affecting 8.8 per cent of all those examined and comprising 60.3 per cent of all dermatoses found. The complete list of dermatoses, in the order of frequency, is as follows:

Dermatosis	Number of Cases
Acne	384
Warts	48
Common warts	5
Plantar warts	41
Filiform warts	2
Nevi	48
Naevus spilus	12 (more than 25 to a person)
Verrucous nevus	9
Pigmented nevus	7 (palm sized or larger)
Naevus flammeus	6 (palm sized; involving lower lids in 2)
Hairy nevus	5 (2 to 4 inches [5 to 10 cm.])
Naevus araneus	5 (many lesions)
Hemangioma	4
Dermatophytosis (clinical diagnosis only)	45
Anomalies of the tongue	16
Geographic tongue	10
Scrotal tongue	6

From the Queens General Hospital and Jamaica Hospital, Dr. Ida J. Mintzer
attending dermatologist.

Dermatosis		Number of Cases
Pigment anomalies		14
Lentigo	10	
Vitiligo	3	
Café au lait spots	1	
Seborrheic eczema (4 of scalp)		10
Herpes simplex		9
Tinea circinata		8
Ichthyosis		7
Hypertrichosis		6
Eczema (generalized)		4
Impetigo		4
Roentgen ray dermatitis (following treatment of nevi)		4
Neurodermatitis (3 generalized)		4
Erythema		3
Keratosis pilaris		3
Keloids (extensive, mostly due to burns)		3
Perlèche		3
Comedos		2
Allergic dermatitis of lip and surrounding skin		2
Psoriasis		2
Subcutaneous fibroids		1
Dermatitis venenata (poison ivy)		1
Lymphangitis		1
Urticaria		1
Multiple benign cystic epithelioma		1
Acute burn		1
Web toes		1
Hyperhidrosis		1
Onychogryposis		1

For purposes of comparison, the dermatoses most frequently found in my series are listed in the accompanying table beside those most frequently found by Goodman,¹ in a large series covering patients of all ages, by Sohrweide,² who surveyed 138,960 cases from the Stuyvesant Square Hospital in New York, by Arena and Harris,³ in the records of 80,000 children under 15 years of age admitted to Baltimore hos-

1 Goodman, H. Tinea. Second Most Prevalent Disease of the Skin, *Arch Dermat & Syph* **23** 872 (May) 1931

2 Sohrweide, A. W. Recent Changes in Dermatologic Diagnosis, *Arch Dermat & Syph* **30** 260 (Aug) 1934

3 Arena, J. M., and Harris, R. R. Frequency and Distribution of Diseases in Children, *South Med & Surg* **97** 520 (Sept) 1935

pitals; by Alderson and Reich⁴ and by Gilman,⁵ each from records of the students' health service at a large university, and by Meyers,⁶ who reported the frequency of diseases in 7,352 boys in continuation school.

None of these series is strictly comparable to mine, as all of them (except that of Meyers) included only persons requesting treatment, and medical care is rarely sought for some of the common dermatoses. Only a small section of Meyers' report is devoted to statistics on cutaneous diseases, and his list is not extensive; it is included, nevertheless, because it covers young adolescents within the same approximate age limits as those in my series and is not confined to those seeking medical care. The valuable earlier statistical survey⁷

Comparison of the Dermatoses Most Frequently Found in Persons at Various Ages

Goodman	Sohrweide	Arena and Harris	Alderson and Reich	Gilman	Meyers	Mintzer *
All Ages	All Ages	Under 15 Years of Age	College Age	College Age	High School Boys	High School Girls
Eczema	Dermatitis venenata	Eczema	Tinea	Tinea	Acne	Acne
Tinea	Eczema	Impetigo	Pyoderma	Acne	Eczema	Warts
Scabies	Acne	Scabies	Dermatitis venenata	Seborrhea	Warts	Nevi
Psoriasis	Tinea	Allergic dermatitis	Seborrhea	Pyoderma	Scabies	Dermatophytosis
Seborrhea	Seborrhea	Pediculosis	Acne	Dermatitis venenata	Herpes simplex	Seborrhea
Impetigo	Impetigo	Ringworm	Warts	Eczema	Trichophytosis	Herpes simplex
Urticaria	Warts	Urticaria	Sebaceous cyst	Pityriasis rosea	Ichthyosis	Tinea
Dermatitis venenata	Scabies	Intertrigo	Urticaria	Moles	Psoriasis	Hypertrichosis
Alopecia	Psoriasis	Angioma	Pediculosis pubis	Herpes zoster	Pityriasis rosea	Eczema
	Alopecia	Erysipelas	Herpes simplex			Impetigo
	Pruritus	Millaria				Roentgen ray dermatitis
	Pediculosis	Burns				Neurodermatitis
		Dermatitis venenata				
		Herpes simplex				

* I have omitted from this list the anomalies of pigment and of the tongue, as these seem not to have been included in the other surveys. It seems likely, too, that some of the other investigators may not have included the common nevus.

of Crocker, Bulkley, Pollitzer (based on the figures of the American Dermatological Association over a period of nearly half a century) and the skin and Cancer Unit of the New York Post-Graduate Medical

4. Alderson, H. E., and Reich, A.: Incidence of Dermatoses in Student Health Service, Arch. Dermat. & Syph. **36**:57 (July) 1937.
5. Gilman, R. L.: Incidence of Skin Diseases in Student Health Service, Am. J. M. Sc. **188**:268 (Aug.) 1934.
6. Meyers, J.: Physical Findings in New York Continuation School Boys, Am. J. Pub. Health **21**:615 (June) 1931.
7. Goodman, H.: Statistics of Ten Most Common Skin Diseases, Based on Analysis of 973,090 Published Cases, Arch. Dermat. & Syph. **20**:186 (Aug.) 1929.
- Crocker, H. R.: Diseases of the Skin, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1903, p. 1401.
- Bulkley, L. D.: Manual of Diseases of the Skin, New York, Paul B. Hoeber, 1898, p. 41.
- Pollitzer, S.: American Dermatological Association, J. Cutan. Dis. **32**:312 (April) 1914; **36**:294 (May) 1918.

School and Hospital have been purposely omitted, since the purpose here is to compare the frequency of dermatoses in adolescents with that in persons of other ages during approximately the same period

It is interesting to note that Alderson and Reich pointed out that acne, although fifth in frequency on their list, is actually present in one half of all students of college age, although comparatively few seek medical care for this cause. Differences in the terminology and classification used in these statistical studies make it difficult to compare the order in the different age groups with absolute accuracy, but it is apparent that the adolescent period is distinguished especially by the increased frequency of warts in the early years, in addition to the expected frequency of acne, with tinea assuming greater importance in the later years of adolescence

Clinical Notes

DERMATITIS DUE TO AQUAPHOR

Report of a Case

S. J. FANBURG, M.D., NEWARK, N. J.

Aquaphor has been used and is used extensively in this country and abroad as an ointment base. It has several advantages over other ointment bases in that it keeps indefinitely and is readily miscible with three times its own weight of water. It is particularly suitable for application to the scalp on account of the ease with which it may be washed out of the hair. It is stated by the manufacturers that aquaphor is a mixture of a group of alcohols and esters of cholesterol obtained from wool fat, 6 parts, in a petrolatum base, 94 parts. The constituents of the mixture are melted together at a certain temperature.

No reports of dermatitis due to aquaphor have come to my notice in the literature. Several cases of sensitization to wool and to wool fat have been reported by Lord,¹ Hertslet,² Ramirez and Eller³ and Sulzberger and Morse.⁴ Beerman⁵ had a wool-sensitive patient who had a flare-up in her dermatitis due to the application of nivea cream, which is a perfumed mixture of aquaphor and water. There are no doubt many unreported or unrecognized cases of sensitivity to wool fat and possibly to aquaphor. Irritation, when it does occur, may be erroneously ascribed to other ingredients of an ointment rather than to its base unless patch tests to determine its exact cause are carried out. The following patient, whom I observed some time ago illustrates sensitivity to aquaphor and to the cholesterol esters contained in it.

REPORT OF CASE

X. B., a white man aged 35, a chiropodist, had pityriasis of the scalp, for which he had used an ointment consisting of 5 per cent salicylic acid and 5 per cent sulfur in petrolatum. He applied this ointment for several weeks and then began the use of one containing 5 per cent salicylic acid and 5 per cent sulfur in aquaphor. Within twenty-four hours after the application of this ointment he noticed a tightness and itching of the scalp, which was soon followed by swelling and vesiculation. The eruption spread to the face, eyelids and ears. The eyes were swollen shut, and the forehead and ears were covered with an erythematous vesicular eruption. The salicylic acid or the sulfur was suspected of being the offending agent. After

1. Lord, L. W.: Cutaneous Sensitization to Wool, *Arch. Dermat. & Syph.* **26**: 707 (Oct.) 1932.
2. Hertslet, L. E.: A Case of Allergic Dermatitis Due to Wool, *South African M. J.* **8**:182 (March 10) 1934; abstracted, *Bull. Hyg.* **9**:379 (June) 1934.
3. Ramirez, M. A., and Eller, J. J.: The "Patch" Test in "Contact Dermatitis" (*Dermatitis Venenata*), *J. Allergy* **1**:489 (Sept.) 1930.
4. Sulzberger, M. B., and Morse, J. L.: Hypersensitiveness to Wool Fat, *J. A. M. A.* **96**:2099 (June 20) 1931.
5. Beerman, H.: Personal communication to the author.

two days' treatment with boric acid compresses, the edema and vesiculation subsided, and an ointment was prescribed which contained 5 per cent boric acid and 10 per cent distilled water in aquaphor. Within two hours after he used this ointment the edema and vesiculation reappeared, the eyelids became swollen and the ears and scalp became acutely inflamed. With the aid of wet dressings the eruption again gradually subsided.

Patch tests were carried out to determine the ingredient of the ointments which caused the dermatitis. Aquaphor itself and any of the ointments containing it gave strongly positive reactions, consisting of vesicles and erythema, in twenty-four hours. Patch tests with petrolatum, hydrous wool fat, sulfur and salicylic acid all gave negative results. Patch tests were performed with the purified cholesterol esters and the petrolatum used in the manufacture of aquaphor. The cholesterol esters produced a vesicular reaction within twenty-four hours. It is interesting to note that the patch test with hydrous wool fat itself, the source of the cholesterol esters, gave negative results.

SUMMARY

A case is presented in which sensitivity to aquaphor and to the purified cholesterol esters used in the manufacture of aquaphor was demonstrated. The patient was not sensitive to wool fat from which the cholesterol esters are derived.

DISCOLORATION OF THE NAILS DUE TO NAIL ENAMEL

HAROLD SHELLOW, M D, CHICAGO

With the advent of "improved" nail enamels and their new color shades, many more complaints have been ushered in concerning the effect these cream polishes have on the nails. More commonly now women have called attention to brittleness, splitting and peeling of the nails, especially at the ends, despite the fact that the customary polish removers, such as acetone and ethyl or amyl acetate, have been used. Various disturbances affecting the nails from the use of nail lacquers have been noted from time to time. I wish to report a both interesting and unusual observation relating to the effect this form of cosmetic has had on the nails.

REPORT OF A CASE

A woman complained of discoloration of the nails of the left hand of about four weeks' duration. She stated that the color, which at first had been a faint red, had gradually increased in tone until its present shade, which was a reddish brown. She had used a popular but not inexpensive nail enamel for some years and had been accustomed to remove the old polish with acetone every week to ten days and then to reapply a fresh coat. She had first noticed the discoloration on removing the polish one day but had reenameled the nails immediately. Each time the old polish had been removed the stain was noticed to have become darker. The nails of the right hand, except for an "acceptable" dryness and scaling of the ends, had been unaffected.

Examination showed a dark orange to reddish brown discoloration of all the nails of the left hand, more pronounced and deeper in color on the first, second

and third nails. The discolored areas were uneven in intensity and less involved on the most proximal and the lateral portions of the nails. The white lunulae were unaffected (these areas had never been enameled). Attempts to remove the stain with several different lacquer solvents failed, even with severe rubbing, but scraping the nails with a glass slide did accomplish some results. However, the keratin was pigmented to such a depth in some nails that it was felt unwise to scrape too deeply for fear of causing injury to the beds.

This asymmetric involvement, of course, was unusual, and in questioning the patient carefully it was brought out that she had been using a prescribed scalp lotion for the previous four weeks. It contained 0.25 per cent mercury bichloride, 1 per cent cholesterol, 2 per cent salicylic acid and 3 per cent resorcinol monoacetate in a 95 per cent grain alcohol vehicle. She had applied this to her scalp each night with her right hand, using a dropper bottle, and then had massaged with her left finger tips.

Apparently some ingredient contained in the scalp lotion had caused a solvent action on the pigment-bearing lacquer, which had permitted absorption of the dye into the keratin. No doubt the friction of the nails against the hair had aided in embedding the stain, and the force with which the longer fingers were used in massaging accounted for the darker color in those nails. For the same reason the peripheral portions were less affected.

185 North Wabash Avenue.

NICOTINIC ACID IN THE TREATMENT OF ACNE VULGARIS

FRANCIS W. LYNCH, M.D., ST. PAUL

One is hesitant to add to the long list of therapeutic agents for use in the treatment of acne, but the disease is so common and the therapeutic results are so mediocre that any help may be welcome. The oral administration of nicotinic acid was suggested by a co-worker's statement that seborrhea appeared to be favorably influenced by this drug. It was then given to 46 university students who had had no previous treatment for acne or no treatment for at least three months preceding their trial of this drug. The nicotinic acid was administered twice daily in the form of 50 mg. tablets taken after the morning and evening meals. No other treatment was used, and the students were given no advice as to diet or hygiene.

The only unpleasant reaction observed in this group of patients was transitory redness, burning or itching in the flush areas of the face, chest and arms. This reaction could usually be avoided by taking the drug immediately after meals.

Eight of the 46 patients failed to present themselves for reexamination. The remaining 38 patients were examined at three or four weeks and again at six to

From the University of Minnesota, Division of Dermatology, Dr. H. E. Michel-son, Director, and the Students' Health Service, Dr. Ruth Boynton, Director.
Part of the material for this study was furnished by The Upjohn Company, Kalamazoo, Mich.

eight weeks In 6 (16 per cent) the results were classed as good and in 15 (39 per cent) as fair, and in 17 (45 per cent) no improvement was noted.

The improvement noted in 55 per cent of patients with acne is not particularly encouraging when one realizes that the disease is cyclic and self limited, so that in any series of patients with acne, whether treated or not, a considerable number will show improvement However, the results in certain cases were so satisfactory that I thought this report was justified Nicotinic acid cannot be regarded as a cure for acne, nor do I hold it responsible for all the improvement noted in these patients, but it is a simple and apparently harmless drug which appears to help

I am unable to explain the mode of action of nicotinic acid, but it may be noted that it is one of the factors in liver, which has been repeatedly advocated in the treatment of acne, and there is some relation between nicotinic acid and the metabolic requirements of the staphylococcus In a few patients the influence on the seborrheic oiliness of the face was most striking

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

ESTHIOMENE—A FORM OF GRANULOMA INGUINALE. A. G. SCHUCH and L. J. ALEXANDER, *Am. J. Syph., Gonorr. & Ven. Dis.* **23**:718 (Nov.) 1939.

The authors report 3 cases of granuloma inguinale associated with elephantiasis and ulceration of the external genitals. They conclude that esthiomene is a clinical entity resulting from various etiologic agents and that the syndrome may be present in cases of granuloma inguinale.

THE LAG IN REVERSAL OF BLOOD SEROLOGIC TESTS UNDER BISMUTH IN THE COURSE OF COMBINED CHEMOTHERAPY. H. BEERMAN, *Am. J. Syph., Gonorr. & Ven. Dis.* **23**:724 (Nov.) 1939.

Studies to a certain degree have borne out the contention that bismuth may have some restraining effect on the arsenical drug in combined arsphenamine and bismuth syphilotherapy. Stokes and Beerman, in their study of trisodarsen (trisodium arsphenamine sulfonate) have obtained, for example, serologic reversal to negative reactions in 90 per cent of cases with this drug alone; while when it was used in combination with bismuth, the serum reaction became negative in three months or less in only 58 per cent of the cases.

The reasons for this possible effect of bismuth compounds may be found not so much in the deterrent action of bismuth on arsphenamine as in the possibility of reduced dosage, intentional or accidental, to eliminate toxicity or because of an inferior drug.

TRISODIUM ARSPHENAMINE SULFONATE (TRISODARSEN) IN THE TREATMENT OF CONGENITAL SYPHILIS. T. B. GIVAN and G. VILLA, *Am. J. Syph., Gonorr. & Ven. Dis.* **23**:771 (Nov.) 1939.

Trisodarsen is a trivalent compound which is chemically known as trisodium arsphenamine sulfonate. Stokes and Beerman were the first to report on this drug, confining their work to cases of early acquired syphilis.

This report deals with a clinical study of the drug in cases of congenital syphilis. The majority of the patients received the drug intravenously, though some were treated intramuscularly. No local reactions were observed. Trisodarsen was relatively well tolerated. Mild reactions, such as nausea and vomiting, occurred, as well as slight cutaneous eruptions in 3 cases and dermatitis exfoliativa in 1 case. Nitritoid reaction was observed in 1 case. No fatality occurred. Patients who had reactions after the administration of neoarsphenamine received trisodarsen without any ill effects.

The drug proved to be effective in the treatment of the various manifestations of congenital syphilis, as well as in producing a negative Wassermann reaction in 76 per cent of 121 patients who had had a positive reaction before treatment.

EARLY SYPHILITIC OSTEOMYELITIS WITH A REPORT OF TWO CASES. U. J. WILE and D. G. WELTON, *Am. J. Syph., Gonorr. & Ven. Dis.* **24**:1 (Jan.) 1940.

Two cases illustrating extensive syphilitic osteomyelitis during the early period of (acquired) infection are presented. In these cases the condition responded satisfactorily to antisyphilitic therapy and showed evidence of complete recovery. Roentgenologic follow-up in 1 case showed no residua of the previous severe (skull) involvement.

THE MENSTRUAL CYCLE AND THE BLOOD SEROLOGIC TEST FOR SYPHILIS N R INGRAHAM and V R MAYER, *Am J Syph, Gonorr & Ven Dis* 24 23 (Jan) 1940

As a result of their studies, the authors concluded that the false positive reactions to serologic tests occurring in some women during the menstrual cycle must result from a peculiarity of the person or of the test and do not arise from any uniform changes in the blood of all women. If occasional exceptional cases occur, their incidence can be deduced only by studies of large groups, beyond the scope of this effort.

THE WASSERMANN TEST XVII THE EFFECT OF ANTISYPHILITIC DRUGS UPON THE WASSERMANN REACTION D L BELDING, *Am J Syph, Gonorr & Ven Dis* 24 29 (Jan) 1940

The reduction of the Wassermann antibody titer was recorded quantitatively during and after treatment of 233 syphilitic patients who were given various preparations of arsphenamine, mercury and bismuth.

In patients with late acquired syphilis an average reduction of the Wassermann antibody titer of 37 per cent was obtained with all the drugs except mercury (used alone), which gave 29 per cent.

The rate of serologic reduction was fairly uniform for all the drugs and reached a maximum at about the twelfth week after treatment. With arsphenamine therapy the serologic reduction in cases of early syphilis was nearly twice that in cases of late syphilis, and the response was more rapid. Bismuth gave the best serologic results in cases of cerebrospinal syphilis.

EMBOLIA CUTIS MEDICAMENTOSA M B SULZBERGER and R L BAER, *Am J Syph, Gonorr & Ven Dis* 24 50 (Jan) 1940

A case of severe embolia cutis medicamentosa is reported which was not caused by an antisiphilitic drug. The common mechanism in the production of the condition is the direct injection of the drug into the artery, as the result of a technical error. However, even with the correct technic of intramuscular injection, an occasional instance of embolia cutis medicamentosa has been reported. It is believed that in such cases the drug is injected into or close to the wall of an artery and that subsequently necrosis of the vessel wall takes place, thus releasing the "stored" drug into the lumen of the artery.

THE PATHOLOGY AND PATHOGENESIS OF SYPHILITIC PRIMARY OPTIC ATROPHY J E MOORE and A C WOODS, *Am J Syph, Gonorr & Ven Dis* 24 59 (Jan) 1940

The authors of this paper critically examined the recent literature on the pathology and pathogenesis of syphilitic primary atrophy of the optic nerve. It appears that this condition is not due to actual syphilitic inflammation of the optic nerves dependent on the presence therein of the causative organism. The newer theories as to its pathogenesis are discussed.

To the authors it seems probable that the pathogenesis of syphilitic primary atrophy of the optic nerve, so often (perhaps almost always) associated with tabes dorsalis, is identical with that of tabes dorsalis itself. This theory, in turn, is as yet unproved, though recent studies, especially in the field of nutrition, offer hope of its elucidation.

REUTER, Milwaukee

LOCAL HEMORRHAGIC-NECROTIC SKIN REACTIONS IN MAN (SHWARTZMAN PHENOMENON) J HARKAVY and A ROMANOFF, *J Allergy* 10 566 (Sept) 1939

The Schwartzman phenomenon is a local cutaneous reaction (hemorrhagic necrotic lesion) following injections of homologous and heterologous filtrates of

various organisms as well as of unrelated antigen-antibody complexes. The first injection is intracutaneous and is termed the preparatory factor; the second is intravenous and is called the provocative factor.

The authors observed 3 patients, 1 with bronchial asthma, a second with hay fever and a third with dermatophytosis and sinus infection in whom developed hemorrhagic-necrotic lesions of the skin. In every case the preparatory factors originated from bacterial foci in infected sinuses and in 1 instance presumably from an additional fungous infection of both feet. The provocative factors consisted of homologous and heterologous proteins composed of bacterial vaccines and toxin filtrates and, in 1 case, antuitrin-S, an unrelated antigen-antibody complex. Since the steps in the evolution of these lesions conform to the criteria postulated by Schwartzman for the production of the phenomenon described by him, the authors regard the hemorrhagic-necrotic lesions in these patients as clinical examples of the Schwartzman phenomenon.

THE PROPHYLAXIS AND TREATMENT OF POISON IVY DERMATITIS WITH AN EXTRACT OF RHUS TOXICODENDRON. L. ZIMMERMAN and L. BIRCH, *J. Allergy* 10:596 (Sept.) 1939.

Individual histories were taken and examinations were made of 1,731 boy scouts, who remained for one or two weeks at a camp where the poison ivy plant (*Rhus toxicodendron*) flourishes with great vigor.

A group of 304 boys and adult leaders, 95 per cent of whom were between the ages of 12 and 17 years, were given prophylactic injections of a special extract of *Rhus toxicodendron*, prepared by extracting the plant with ether and then suspending the extracted material in a 1:1,000 dilution of olive oil. The dose varied from 0.25 cc. to 1 cc. Some boys received only one injection, and others received two injections at weekly intervals.

A history of previous susceptibility was given by 241 of the treated boys. Of these, poison ivy dermatitis developed in 146 while they were in camp, an incidence of 60.6 per cent. The general incidence in the camp for the reacquisition of the dermatitis during the study period among known susceptible subjects was only 47.6 per cent, showing a lessened immunity as a result of prophylactic injections rather than the acquisition of any immunity.

Eighty-nine boys in whom poison ivy dermatitis developed were treated with a 1:10,000 dilution of antigen. Patients were given one, two or three injections at daily intervals in doses of 0.25 cc. and 0.5 cc. Few of the patients treated had the prophylactic injections. No local therapy was given. The results were unsatisfactory in 29 patients; 21 were relieved of the itch; 30 were improved, and in 9 the results were good.

THE TRANSFERENCE OF REAGINS IN BLOOD TRANSFUSIONS. W. P. GARVER, *J. Allergy* 11:32 (Nov.) 1939.

The author observed 3 nonallergic recipients whose skin was passively sensitized after the transfusion of whole blood from allergic donors.

The first donor had perennial allergic vasomotor rhinitis, with seasonal exacerbations due to weed pollens. His skin was sensitive to house dust, chocolate, string beans, spinach and ragweed. He acted as a donor for 2 recipients.

Before transfusion the recipients were given cutaneous tests with all of the substances except house dust; the reactions were negative. After the transfusions of 500 cc. of blood, the recipients were again tested with the same substances; it was found that they reacted to ragweed, string beans and spinach. These substances gave positive reactions with the donor's blood by the Prausnitz-Küstner technic of passive transfer. The reactions in the recipients were maximum in four to five days and remained positive for about two weeks. After this time they were faint and difficult to interpret.

The second donor had late hay fever, and his skin was sensitive to house dust, orris root, horses and timothy and ragweed pollen. He acted as a donor for a

recipient in whom cutaneous tests gave negative reactions to the above allergens before transfusion. Fourteen hours after a transfusion of 500 cc of whole blood, the recipient's skin showed slight reactions to house dust and ragweed. In four days the reactions were moderate to severe to all the allergens. On the sixth day the reactions were not as severe as they were two days previously.

No attempt was made in any of these cases to demonstrate clinical sensitivity.

NOTE ON ORAL POTASSIUM CHLORIDE THERAPY IN ASTHMA, HAY FEVER, URTICARIA, AND ECZEMA DAVID HARLEY, *J Allergy* **11** 38 (Nov) 1939

Oral potassium chloride therapy, in doses of 5 grains (0.32 Gm) dissolved in a glass of water and given one-half hour before meals three times a day, failed to produce a significant degree of improvement in a group of 43 allergic patients. These included patients with hay fever, allergic rhinitis and asthma, 10 with each, 9 patients with urticaria and 4 patients with eczema. The average duration of treatment was from two to three and four-fifths weeks.

In 1 case of urticaria, in which there was moderate improvement, relapse occurred in four weeks. There was favorable response, however, to a course of sodium chloride tablets three times a day in water.

MENDELSON, New York

NICOTINIC ACID IN THE TREATMENT OF ACRODYNIA FREDERICK F TISDALL, T G H DRAKE and ALAN BROWN, *J Pediat* **13** 891 (Dec) 1938

Six infants ranging in age from 8 months to 2 years suffering from acrodynia were treated with nicotinic acid. Two forms of the drug were used, pure nicotinic acid and the monoethanolamine salt of nicotinic acid. No difference was found in the action of these two substances. The drug was administered parenterally in order to obviate any possibility of defective absorption from the intestinal tract. The first dose (20 mg) was given intravenously, and subsequent doses of from 20 to 40 mg were given intramuscularly twice daily. The only reaction noted was redness and blotching of the skin in 2 babies, occurring shortly after the injection and lasting only one-half hour. In a few cases the drug was given by mouth, 100 mg a day being given to the younger and 125 mg a day to the older infants. In addition, all the infants were given a diet consisting of milk, egg yolk, a mixture of equal parts of pabulum, wheat germ and a finely ground green oat grass rich in the vitamin B complex, percomorph liver oil, orange juice and in the cases of the older infants, liver. Nicotinic acid seemed to hasten the healing of the cutaneous lesions, but no evidence was found that it shortened the period of recovery from the disease.

ACRODYNIA TREATED WITH INTRAMUSCULAR INJECTIONS OF VITAMIN B₁ JAY I DURAND, V W SPICKARD and ERNEST BURGESS, *J Pediat* **14** 74 (Jan) 1939

Two cases of acrodynia are described. Three days after treatment with intramuscular injections of vitamin B₁ was begun, marked improvement occurred. In both cases the improvement ceased and the symptoms grew worse when the injections were discontinued and the vitamin was given by mouth. In spite of the relapses which recurred when treatment by mouth was given, both patients recovered in six weeks from the beginning of injection treatment.

RAUH, Cincinnati [AM J DIS CHILD]

SCLERODERMA IN BANDS AND PARATHYROIDECTOMY W NAESSENS, *Maandschr v kindergeneesk* **8** 173 (Feb) 1939

Naessens gives a description of extensive and progressive scleroderma in bands in a girl of 11 years. Extirpation of a parathyroid gland resulted in amelioration, which lasted for about nine months. The author is of the opinion that the

sclerodermic syndrome does not have its cause wholly in the parathyroids. Parathyroidectomy may explain why the calcium has returned from the calcified skin to the decalcified skeleton.

A CASE OF BESNIER-BOECK DISEASE. A. VON WESTRIENEN, *Maandschr. v. kindergeneesk.* 8:262 (April) 1939.

A girl of 13 years presented Besnier-Boeck disease. There was swelling of all superficial groups of lymph nodes, and there were numerous subcutaneous small tumors, also knotty parotid glands and slight deviations in the cornea and in the capsule of the lens. A roentgenogram of the lungs showed the typical pseudo-miliary picture, with severe enlargement of the lymph glands. The phalanges showed small deviations. Biopsy of a lymph node and of a subcutaneous tumor, which appeared to be situated in the muscular tissue, confirmed the diagnosis. The therapy consisted in administration of arsenic and rest in bed. The tumors and the lesions in the lungs soon disappeared. The results of tuberculin tests were negative, as they generally are in analogous cases.

SCLEREMA ADIPOSUM NEONATORUM. C. GOEDHART, *Maandschr. v. kindergeneesk.* 8:281 (April) 1939.

Goedhart describes histologic changes in the skin of a baby suffering from "sclerema adiposum." In the cutis and subcutis streptococci were abundant, especially in the lymph vessels. Many capillaries were distended and filled with blood. The greatest changes—among others, "necrosis"—were around the adipose tissue, so that the impression gained was that the streptococcic toxins had caused special changes in this tissue and in this way the hardness of the skin. On the right cheek the child showed an infection looking like a mosquito bite. The mother had latent syphilis with positive blood reactions. No signs of syphilis and no spirochetes were found in the child, not even in the organs. A second patient, a child, died within three days from streptococcic sepsis.

CONGENITAL CUTANEOUS DEFECTS CAUSED BY A FORM OF EPIDERMOLYSIS BULLOSA. J. R. PRAKKEN, *Nederl. tijdschr. v. geneesk.* 83:2440 (May 27) 1939.

A child when born presented two blisters, which developed into slowly scarring cutaneous defects. Taking into consideration several other observations in the literature, Prakken states that this case supports the opinion that a number of congenital defects of skin may result from a form of epidermolysis bullosa congenita. How far this form is connected with the known varieties of epidermolysis bullosa hereditaria cannot yet be answered. The probability of epidermolysis congenita being in some cases the origin of congenital defects of skin was mentioned first by Carol and Heybroek, in 1925.

TREATMENT OF CUTANEOUS PRURITUS WITH INSULIN. C. G. VERVLOET, *Nederl. tijdschr. v. geneesk.* 83:2728 (June 10) 1939.

Insulin has been shown to exert a great therapeutic influence in several forms of cutaneous pruritus. This probably depends on correction of the intracellular metabolism in the liver and in the kidneys. This medication is recommended for different types of itching of the skin.

VAN CREVELD, Amsterdam, Netherlands. [AM. J. DIS. CHILD.]

Society Transactions

LOS ANGELES DERMATOLOGICAL SOCIETY

CHRIS R HALLORAN, M D, *Chairman*

SAUL S ROBINSON, M D, *Secretary*

Feb 13, 1940

Chronic Roentgen Ray Dermatitis of the Hands, Arms and Legs, with Epithelioma Presented by DR C RUSSELL ANDERSON

Mrs V E, a housewife aged 53, had roentgen ray epilation of the hair on the legs and the forearms six years ago. Six to twelve months later she noticed that the treated skin was red. On April 1, 1938 she noted a small ulceration on the right forearm. This healed and recurred and spread almost over the length of the forearm.

A dermatologic examination on October 14 revealed pigmentation, atrophy, telangiectases, papillary elevations, scaling and keratotic lesions on the dorsal surfaces of the forearms and legs. On the right forearm was a crusted, ulcerated area, 12.5 cm long and 1 to 4 cm wide, with scleroderma-like induration. On Feb 9, 1939 the patient returned with multiple crusted and ulcerated areas on the left forearm near the elbow. There were also multiple new keratoses on other involved regions. On November 13 the ulcerated area on the right forearm and the multiple keratoses were removed by the cautery. The microscopic examination showed chronic roentgen ray dermatitis, ulceration and early squamous cell epithelioma.

On Feb 2, 1940 a biopsy specimen was taken from the papillary lesion just adjacent to the ulcerated area of the left forearm. The histologic examination showed hyperkeratosis, granulosis and thickening of the prickle cell layer. There were some areas of tinctorial change, with irregularity in size and shape of the cells, evidences of amitosis and cells with large, deep staining nuclei. The cutis showed fibrosis, homogenization of collagen, dilated vessels and absence of dermal appendages. The histologic diagnosis was chronic roentgen ray dermatitis, with early squamous cell epithelioma.

DISCUSSION

DR L F X WILHELM I have not observed any cases of radiodermatitis in four or five years. In New York during the years 1925-1926 as many as 4 or 5 cases of roentgen ray dermatitis were presented at one meeting.

DR CHARLES R CASKEY I should like to suggest a method of therapy. I have had a patient with a similar condition under observation and treatment for ten years. The hands, arms, legs and feet had extensive telangiectasia. The patient is a school teacher, and her hands were getting so bad that something had to be done. I used a light electrodesiccation spark and followed the telangiectases with a small spark. It is surprising to see how much benefit can be derived by this method of treatment. Some of the vessels will break and bleed, and an astringent is necessary. One should begin by treating the smaller telangiectases first. The electrodesiccation machines that give a black, charred spot are not satisfactory. One should have the current light enough to get a white desiccated area which closes up the telangiectases. My patient comes in the office for treatment only once or twice a year now. Two or three epitheliomas developed in some of the worst areas, and these have been treated with the cautery.

DR. C. RUSSELL ANDERSON: I thought the case would be interesting because of the extensive involvement. Cautery excision of the ulcerated areas is to be performed this week.

Sarcoid of Boeck with Uveitis and Keratitis. Presented by DR. C. RUSSELL ANDERSON.

Mrs. L. A. S., aged 64, was first seen on July 25, 1939. The history disclosed that in 1914 tuberculous glands were removed from the left side of the neck. In 1927 her eyes became "inflamed" and cleared after a cholecystectomy. In 1936 the ocular complaint recurred. Tuberculin tests performed in May 1936 gave strongly positive results and produced a flare-up of the ocular condition. A diagnosis of tuberculous keratitis was made. From 1936 until early in 1939 the patient received many subcutaneous injections of tuberculin. These injections occasionally produced an exacerbation of the ocular condition. During the latter part of February 1939 a red, slightly elevated plaque appeared on the upper lip, with obliteration of the normal lip markings.

The dermatologic examination on July 25 showed an oval, infiltrated, moderately elevated, reddish brown, slightly scaling plaque on the upper lip. The lesion was 4 by 2.5 cm. in size. It involved the philtrum, with obliteration of the normal markings, and the left side of the upper lip. The diascopic examination showed bilateral keratitis and argyrosis of the upper and lower lids. Examination of the ear, nose and throat revealed normal mucosa on the nasal septum and an extremely large left middle turbinate, interpreted as concha bullosa. Roentgenograms of the hands on August 24 revealed no cystic changes in the phalanges. The roentgenogram of the chest showed several small densities in the outer half of the right and left first and second interspaces, suggestive of old healed tuberculous processes. There were also some densities in the hilar processes. The blood and urine were normal. Flocculation tests for syphilis gave negative results. The histologic examination revealed round, oval and irregular masses of epithelioid cells in the cutis. An occasional Langhans giant cell was found. There was no caseation necrosis.

The treatment consisted of the administration of seventeen weekly injections of gold sodium thiosulfate. The doses varied from 20 to 50 mg. There was a rapid initial response in the cutaneous lesion. The sarcoid became smaller and less infiltrated, and there was a return of the normal contours of the philtrum. The ocular condition has also responded well to the gold therapy.

DISCUSSION

DR. WILLIAM H. GOECKERMAN: I have to take Dr. Anderson's word that the findings were as he said. I cannot see enough tonight to make a diagnosis of sarcoid, but the combination is a common one, and I readily accept the diagnosis.

DR. SAUL S. ROBINSON: I saw this patient before the gold therapy was given. The lesion clinically was sarcoid. I followed the case closely when Dr. Anderson was giving treatment, and there was a definite improvement each week.

DR. C. RUSSELL ANDERSON: There is little to see in the limited artificial light. However, in daylight there is still a brownish red color visible, and also a small amount of infiltration is palpable. The therapeutic result is good, but I feel it can be improved.

Senear-Usher Syndrome (Pemphigus Erythematodes; Chronic Benign Familial Pemphigus; Herpetiform Dermatitis Repens of Ayres and Anderson). Presented by DR. C. RUSSELL ANDERSON.

A. H. N., a man aged 32, states that about two months previously a scaling, moist, crusted, tender eruption associated with increased sweating appeared in the armpits. The right axilla was especially involved. Calamine lotion N. F. and a naftalan ointment were applied, without benefit.

The dermatologic examination showed many irregularly oval, crescentic, moist, scaling, crusted and vegetating patches in the right axilla. Ruptured bullae were present. In the borders of the scaling, crusted and vegetative patches were seen herpetiform lesions. The left axilla was similarly but less extensively involved. The presence of the bullae and the vegetating lesions suggested pemphigus vulgaris, but the herpetiform lesions supported the diagnosis as presented.

The therapy consisted of a drying paint containing 5 per cent coal tar solution. From Dec 18, 1939 to Feb 9, 1940 eight weekly superficial roentgen ray irradiations (75 r) were given to the lesions, together with weekly intravenous administrations of 1 Gm calcium gluconate. Within eight days the lesions in the left axilla and the hyperhidrosis disappeared, leaving a reddish brown pigmentation. The vegetating lesions in the right axilla rapidly disappeared. The red, scaling, crusted, moist patches and herpetiform character remained, although they were greatly improved.

Recurrent Herpetiform Dermatitis Repens Presented by DR SAMUEL AYRES JR and DR JOHN D ROGERS (by invitation)

C R, a white man aged 31, has had a recurrent, pruritic, painful eruption on the head and neck for sixteen years. The lesions appear for one to six months of each year regardless of the season. The present eruption is located on the neck and is of one month's duration. The eruption starts as erythematous maculopapular lesions, which are followed by vesicles. There is no history of the ingestion of drugs.

The examination shows vesicular and bullous lesions on an erythematous base, 0.5 to 2 cm in diameter, located especially on the dorsum of the neck. The borders are irregular, and the centers are raised. Crusts are present. The examination of the blood and urine gave negative results.

DISCUSSION

DR SAMUEL AYRES JR: Brief examination of the last 2 patients suggests that this disease resembles the one we reported on recently, especially the patient who presented lesions on the neck (*ARCH DERMAT & SYPH* 40:402 [Sept] 1939). I do not wish to go on record without an opportunity of further examining this patient. The lesions on the neck were healed. They are frequently herpetiform in the beginning, then they spread out as a moist process. I have not the least idea as to the causation. It might be worth while to give nicotinic acid a trial. I think that in the case with the lesions in the axillae the condition is of too short duration to make a diagnosis. It may develop into a true dermatitis herpetiformis. The process in the second case, however, has been going on for sixteen years. I think this case is a typical one of the group of diseases as presented.

DR C RUSSELL ANDERSON: It is certain that this condition is not a new entity but only an old one which was never completely understood. At the present time eight or ten or probably more names have been given to this syndrome, as I mentioned in the presentation. The reason for the multiplicity of names is that different authors have described different clinical manifestations. The condition when limited to intertriginous areas has even been treated as chronic moniliasis by competent dermatologists. Now that almost every one is familiar with the syndrome and its protean clinical manifestations, its benignancy, its chronicity and its occasional familial occurrence, one name should be adopted for it. I believe that either Senear-Usher syndrome or Senear-Usher pemphigus should be adopted as the proper designation, because these authors first attempted to describe the syndrome (Senear, F E, and Usher, B. *An Unusual Type of Pemphigus*, *ARCH DERMAT & SYPH* 13:761 [June] 1926). The original article demands rereading and is especially recommended to any authors who are attempting to describe a new disease. As to treatment, superficial roentgen irradiation and intravenous injections of calcium salts have given me the best results.

DR. KENDAL FROST: Dr. C. Russell Anderson mentioned the use of calcium intravenously. I have used it in my case, and it seems to lessen the eruptive tendency of the lesions but is not, of course, curative.

DR. NELSON PAUL ANDERSON: I suggest that anybody who presents a case of what is believed to be benign familial pemphigus should present a biopsy slide. I believe that time will demonstrate that this disease has a characteristic histologic picture. Recently there have been three separate communications from widely separated parts of the country, all of which were describing the same entity (Pels, I. R., and Goodman, M. H.: *ARCH. DERMAT. & SYPH.* 39:438 [March] 1939; Hailey, H., and Hailey, H., *ibid.* 39:679 [April] 1939; Ayres, S., and Anderson, N. P.: *ibid.* 40:402 [Sept.] 1939). Pels wrote on a peculiar type of Darier's disease with bullae, which is certainly the same sort of process as in Drs. Ayres and Rogers' case. Hailey and Hailey stated the belief that the condition is benign familial pemphigus because of its familial trait. I think they have a family group with 6 cases. The picture that Dr. C. R. Anderson's patient presents as one of the Senear-Usher syndrome or benign familial pemphigus might be either one of these conditions, but I do not believe that these two terms can be used synonymously.

DR. CHRIS R. HALLORAN: In the past year 3 or 4 patients with this dermatosis have been presented before this society. Hailey and Hailey (*ARCH. DERMAT. & SYPH.* 39:679 [April] 1939) reported the first cases under the title "Familial Benign Chronic Pemphigus." Ayres and Anderson presented a report of 5 cases at the sixty-eighth annual meeting of the California Medical Association, Del Monte, Calif., on May 1, 1939, under the title "Recurrent Herpetiform Dermatitis Repens." In my opinion this form of pemphigus does not belong to those forms designated as the Senear-Usher syndrome. I also believe that clinically this entity can be definitely differentiated from other clinical forms. Apparently the condition in these cases represents a new benign form of pemphigus.

DR. SAMUEL AYRES JR.: I saw Dr. Frost's patient many years ago, and then I did not see any one with a similar condition until five or six years ago. It seemed to me that the condition in this case belongs in the same category. I do not believe it is the Senear-Usher syndrome, because the lesions occur on the neck and folds of the axillae and their appearance is not that usually seen in cases of Senear-Usher disease.

Naevus Flammeus. Presented by DR. CHARLES R. CASKEY.
D. B., a boy aged 3, has had a port wine mark on the right temporal region since birth. The mother has a similar type of birth mark. He is shown after treatment of the lesion with solid carbon dioxide.

DISCUSSION

DR. SAMUEL AYRES JR.: I think this cosmetic result is beautiful, as naevus flammeus is notoriously difficult to treat. When treatment is started in a small child, the results are apt to be better. I treated a little girl two years ago and did not succeed in getting rid of the nevus, but the father later said that the treatments started the child stuttering, due to "psychic trauma." The child had not talked before.

DR. CHARLES R. CASKEY: This patient has been under treatment since February 1938. The last treatment was given six weeks ago. He has had seventeen treatments. I should freeze the lesion with carbon dioxide and leave it alone for a month or six weeks and then refreeze it. I used an exposure of twelve to eighteen seconds with slight pressure and increased the time or pressure or both when necessary to cause sufficient sclerosis.

Basophilic Adenoma of the Pituitary. Presented by DR. NELSON PAUL ANDERSON.
H. A., a Negress aged 15, was first seen in the endocrine department of the Yale Street Clinic, where a diagnosis of thyroid and pituitary dysfunction was

made The examination reveals obesity, particularly of the arms, the thighs and the trunk There are striae distensae on the thighs, arms and lateral aspects of the trunk

The laboratory examinations showed the blood and urine to be normal, the basal metabolic rate plus 2 per cent, water balance 6 per cent and sedimentation time 34 mm per hour The roentgenogram of the wrist showed the bones to be normal for the patient's age

Perifolliculitis Capitis Abscedens et Suffodiens, Cutis Verticis Gyrata, Hydradenitis Suppurativa Presented by DR NELSON PAUL ANDERSON and DR MILTON STOUT (by invitation)

P N, a Negro aged 28, has had gyrations on the scalp all his life Four years ago abscesses appeared over the occipital region These abscesses were incised and drained and required six to eight weeks to heal One year ago multiple small "abscesses" appeared throughout the scalp, particularly over the occiput These lesions have been repeatedly incised and drained Several months ago "boils" developed in the axillas, groin and perianal region The patient was seen in the dermatologic service of the Los Angeles County Hospital on Jan 25, 1940 At that time over the scalp there were multiple fluctuant areas, of which some were draining and some showed evidence of fibrosis He was admitted to the hospital for examination and treatment

The examination of the blood and urine gave normal results The serologic and flocculation tests of the blood gave negative results Cultures made from the scalp lesions showed a growth of pure *Staphylococcus aureus*

The treatment consisted of the administration of sulfapyridine and nicotinic acid as follows sulfapyridine, 15 grains (1 Gm) every four hours for seven days, 17½ grains (1.13 Gm) every four hours for nine days and 17½ grains (1.13 Gm) every six hours for two days, nicotinic acid, 50 mg twice daily The total dose of sulfapyridine was 73 Gm This maintained a blood level of 4.7 mg per hundred cubic centimeters Under this regimen the drainage ceased and the fluctuant areas became fibrosed, as seen now The hydradenitis suppurativa subsided readily

DISCUSSION

DR WILLIAM H GOECKERMAN I fully agree with the diagnosis I think it is interesting to find these three dermatologic phenomena in the same patient I have long had a feeling that there is a close etiologic relation

Keratosis Follicularis (Darier) with Remission and Exacerbation Presented by DR C RUSSELL ANDERSON

Miss A M, aged 24, was first seen on Feb 12, 1940, and the following history was obtained In December 1938 a brownish, warty, furrowed patch appeared on the dorsum of the left hand between the thumb and index finger Five months later the lesion disappeared spontaneously In December 1939 the patch reappeared No subjective symptoms were present Multiple flat warts have been present on the right hand for two years

On the dorsal surface of the hand, involving the first interdigital space and the web between the thumb and the index finger, is a brownish patch composed of aggregated papules and papillomatous lesions There is furrowing at the sites of the normal cutaneous folds The surface of the lesion is stippled with tiny, cayenne-pepper-like spots Multiple flat warts are seen on the dorsal surface of the right hand and fingers

The histologic examination showed relative and absolute hyperkeratosis, moderate granulosis and acanthosis Dyskeratotic cells were numerous Corps ions and grains were found in all parts of the epidermis, from the basal layer to the granular layer Space formation was absent

DISCUSSION

DR. KENDAL FROST: The peculiar warty lesions were not removed for biopsy. I was surprised when I saw the histologic section. The histologic picture was not characteristic of the diagnosis as presented.

DR. C. RUSSELL ANDERSON: The biopsy specimen was taken late last night with next to the smallest size punch. Apparently some members of this society have had no experience with the extremely simple and satisfactory punch technic for removal of material for biopsy. The interesting thing about this case is the spontaneous remission of Darier's disease and its recurrence after a year.

Acanthosis Nigricans Associated with a Masculinizing Syndrome. Presented by DR. C. RUSSELL ANDERSON.

Miss F. M., a laundry presser aged 30, white, was first seen on Jan. 26, 1940. She stated that when she was 15 a heavy log fell across her abdomen and produced a grapefruit-sized red, painful swelling in the left loin. She was put in a body cast for four months, during which time universal hypertrichosis appeared. Since that time she has menstruated only five times, the last menses, on Dec. 15, 1939, requiring only two pads. For the past four years there has been a profuse, thick, yellow vaginal discharge every thirty days. The breasts failed to develop and became atrophic. On Oct. 13, 1937 the clitoris was amputated. On December 5 bilateral exploratory operation was performed, in a search for adrenal tumors; none were found. After the operation frontal and temporal alopecia appeared. On March 8, 1939 a laparotomy was performed to explore the pelvis. Small masses of ovarian tissue and a small uterus were found. No ovarian tumors were present. During the past six months extreme fatigue, weakness in the arms and hands and an aching pain between the shoulders have been present. These symptoms have been increasing from week to week.

The examination reveals the body conformation to be entirely masculine. The patient is well developed, lean and heavily muscled. There are universal hypertrichosis, a heavy beard and a male type of frontal and temporal alopecia. The breasts are small and undeveloped. A few white striae are present on the anterior aspect of the thighs. Obesity, lividity and acneform lesions are present. The anterior axillary folds are the sites of hyperpigmentation, papillary hypertrophy and parallel rugae in the sites of the normal cutaneous folds. (The presence of these lesions was unknown to the patient until attention was called to them.) The blood pressure is 122 systolic and 80 diastolic; the pulse is 88 per minute. Glycosuria is absent.

The histologic examination of an axillary fold lesion showed typical features of acanthosis nigricans. There were relative and absolute hyperkeratosis, with the epidermis thrown up into folds, acanthosis, with decided prolongation of the rete pegs, and increased pigmentation of the basal cell layer.

DISCUSSION

DR. C. RUSSELL ANDERSON: I thought the case interesting because of the associated acanthosis nigricans. Because of the absence of adrenal or ovarian tumors, I have made a tentative diagnosis of a tumor of an adrenal rest, possibly in the region of the celiac plexus.

Argyria. Presented by DR. SAMUEL AYRES JR.

O. H., a girl aged 5 years, was burned with hot coffee two years ago. She was treated immediately with 5 per cent tannic acid and 10 per cent silver nitrate. After the eschar separated, a pronounced argyria was present. The mother noted that the areas exposed to the sunlight improved in comparison with covered areas and had the patient wear a sun suit. The pigmentation has gradually disappeared.

DISCUSSION

DR SAMUEL AYRES JR I had not seen the patient for two years until the day before yesterday, when the mother told me that she had discovered that while the child was wearing shorts in the summer the areas exposed to the sunlight were paler than the covered parts Taking that for a clue, she exposed all the affected areas to the sunlight, with the result seen tonight It was contrary to what one would have expected One would have thought the pigment would increase rather than decrease I should say that the color had faded 80 to 90 per cent, with no other treatment than exposure to the sun Whether the pigment would have faded anyway, I do not know

CHRIS R HALLORAN, M D, *Chairman*

SAUL S ROBINSON, M D, *Secretary*

March 12, 1940

A Case for Diagnosis (Tuberculosis Cutis? Lupoid Syçosis?) Presented by DR JULIUS R SCHOLTZ

J B, a white man aged 57, has had "lung trouble" and "asthma" for many years He was first seen in September 1938 because of a palm-sized lesion on the left temporal and parietal region The eruption consisted of an erythematous plaque, with many follicular pustules, scarring and alopecia in the involved area The scar was atrophic and telangiectatic The condition was considered to be a mycotic or bacterial infection, but organisms have never been found on microscopic examination or by culture Treatment consisted of the local application of iodine, thymol, anthralin (dihydroxyanthranol) and mercurials, but there was no response to therapy The course of the eruption has been fluctuating, showing sometimes involution and sometimes exacerbation, with the appearance of a new crop of pustules overnight The subjective symptoms consist of some pain and itching There have never been constitutional symptoms or associated lymphadenopathy There is no history of the administration of medicaments

The serologic tests for syphilis gave negative results Histologic examination showed a dense round cell infiltration in the cutis The infiltrate was arranged in fairly well circumscribed masses about the blood vessels and cutaneous appendages The cells consisted entirely of small and large lymphocytes and epithelioid cells There was one small circumscribed group of epithelioid cells, small lymphocytes and fibroblasts that resembled a fairly well developed tubercle

DISCUSSION

DR E D LOVEJOY The picture suggests sycosis, but there is not much scarring I am in favor of the original diagnosis

DR BEN NEWMAN (by invitation) The principal feature of this eruption is pustular folliculitis involving the outer border of the left temporal region of the scalp, with resulting cicatrizing alopecia I consider this case a classic example of lupoid sycosis

DR C RUSSELL ANDERSON I agree with the diagnosis of lupoid sycosis, or, as it is sometimes called, folliculitis sycosiformis atrophicans capillitii

DR H C L LINDSAY I consider the eruption to be follicular, not tuberculous The area is too extensive and too pustular, considering the age of the lesion There is a tendency for lupus to avoid pus formation

DR JULIUS R SCHOLTZ I was not particularly convinced of the correctness of the diagnosis under which I presented the case I had always considered the case to be one of bacterial folliculitis or sycosis, and was surprised to find that

the pustules were sterile on repeated examinations. The diagnosis of tuberculosis was suggested by the biopsy report, but clinically this diagnosis can hardly be considered. It is, nevertheless, interesting that the section shows almost a pure lymphocytic infiltrate. In a pyogenic disease, such as lupoid sycosis, one would expect to find the usual evidences of pyogenic inflammation.

DR. SAMUEL AYRES JR.: I believe that the folliculitis is due to a focus of infection, either tuberculous or streptococcic. The condition is possibly a variant of lupus erythematosus. I have observed cases that present features of both lupus erythematosus and sycosis vulgaris.

DR. A. FLETCHER HALL JR.: I consider the case to be one of ulerythema sycosiforme.

DR. NELSON PAUL ANDERSON: My diagnosis is typical lupoid sycosis.

Myelogenous Leukaemia Cutis. Presented by DR. JULIUS R. SCHOLTZ.

Mr. B. B., aged 56, states that he had an "itching eruption" twenty years ago that responded to roentgen irradiation. He does not know whether a definite diagnosis was made at that time. The present pruritic eruption began eighteen months ago and involves the tip of the nose and the trunk. The lesions have fluctuated somewhat but have never entirely cleared.

The dermatologic examination shows a weeping, crusted eruption involving the nose, the anterior part of the trunk and the left axilla. The primary lesion is an indurated dusky red papule. The papules coalesce and form large, poorly defined patches. The general appearance is that of an infectious eczematoid dermatitis, but hemorrhagic and indurated lesions are present. Splenomegaly and enlarged mediastinal nodes are found on examination. Laboratory examination showed the granular leukocyte count to be as high as 70,000 per cubic millimeter, with reductions after high voltage roentgen irradiation to the spleen. The histologic examination showed grouped and scattered, large, lightly staining leukocytes with poorly defined nuclei in the upper part of the cutis. The leukocytic cells were situated in and about the blood vessels and between the bundles of connective tissue. Some of these cells were three times the size of a polymorphonuclear leukocyte and were probably myeloblasts.

The therapy has consisted of the administration of six fractional doses (60 r) of superficial roentgen rays to the involved cutaneous areas. Some involution of the lesions resulted from this therapy. The patient is also receiving deep roentgen irradiation to the spleen.

DISCUSSION

DR. WILLIAM GOECKERMAN: The lesions are not typical of true leukemia cutis but are probably leukemids.

DR. WALTER SCHWARTZ (by invitation): There is no question of the diagnosis of myelogenous leukemia, but I hesitate to consider the cutaneous lesions as being due to it, because specific cutaneous infiltrations in myelogenous leukemia are extremely rare. I believe that there are only 17 or 18 such cases reported. The patient may be suffering from pruritus, as is seen in most cases of Hodgkin's disease, and the lesions on his skin may be secondary to scratching.

DR. JULIUS R. SCHOLTZ: I have not seen this patient for three weeks, and the picture has changed considerably. When first examined, he presented a weeping, crusted dermatitis involving the nose, the left axilla and the left side of the abdomen, with many scattered crusted papules on the neck and the extremities. The picture looked like an infectious eczematoid dermatitis, but the papules were unusually "shotty." He received superficial roentgen irradiation to the cutaneous areas and high voltage roentgen therapy to the spleen and the lymph glands. It is of interest that the cutaneous lesions showed considerable improvement while the high voltage therapy was being given, during the period before treatment of the skin was begun. The histologic section showed infiltration with cells characteristic of the disease.

Localized Scleroderma. Presented by DR JULIUS R SCHOLTZ

J H, a white man aged 21, has had a thickened area on the abdomen for several years. There is a past history of a severe streptococcic infection of the throat at the age of 6 years. Three months ago he had an infection of the sinuses, necessitating a radical operation on the antrum. After surgical intervention the lesion increased in size.

In the right upper abdominal region, near the umbilicus, is a palm-sized, oval lesion with a white sclerotic central zone, a narrow brown middle zone and an erythematous purple outer area. The central area shows two hard, indurated spots at each end, the shape of a dumb-bell.

The basal metabolic rate was — 6 per cent. The histologic examination showed a thin epidermis with considerable pigment in the basal layer. The upper part of the cutis contained slight perivascular round cell infiltration. The collagen throughout the upper half of the cutis was swollen and blurred. There were homogenization and fragmentation of the collagen bundles.

The treatment has consisted of the daily administration of thyroid, $\frac{1}{2}$ grain (0.03 Gm), and daily olive oil massage of the lesion.

DISCUSSION

DR SAMUEL AYRES JR. I have seen several patients with morphea benefited by treatment with water-cooled ultraviolet irradiation applied with pressure for several minutes to the point of obtaining a blistering reaction. It is true that lesions of scleroderma may heal spontaneously, but I believe that water-cooled ultraviolet radiation with pressure is of benefit.

DR ANKER K. JENSEN (by invitation). I have had under my care at the dermatologic clinic of the White Memorial Hospital a patient with two areas of localized scleroderma. These two areas have received the same amount of treatment, acetylbetamethylcholine hydrochloride (mecholy) iontophoresis. One of these lesions is now soft and pliable, with no sign of induration, the other has not shown much improvement. This treatment has been given twice a week for three months. I wonder if any of the members of the society have used "aciform" (a compound of formic acid, 95 per cent alcohol, iodine crystals, sulfur, terpene and distilled water). Dr Laurence H. Mayers has reported (*Indust Med* 8 443 [Nov] 1939) some interesting results with it in the treatment of scleroderma.

Rosacea-Like Tuberculid. Presented by DR PAUL D FOSTER

Mrs J K M, a housewife aged 46, complains of an eruption on the face, of one year's duration. The lesion first appeared on the cheeks and gradually spread to involve the forehead and the neck. The dermatologic examination shows a fine erythematous papular eruption on the face, especially on the central regions, associated with flushing.

The examination of the blood showed 87 per cent hemoglobin, 4,400,000 erythrocytes per cubic millimeter and a color index of 0.97, with 66 per cent leukocytes, 30 per cent lymphocytes, 2 per cent monocytes and 2 per cent eosinophils. The Kline test gave a negative action.

DISCUSSION

DR STANLEY CHAMBERS. Although the cutaneous picture in this case is not that of the accepted rosacea-like tuberculid, it does represent the atypical types which have been occasionally described.

DR WILLIAM GOECKERMAN. I cannot see anything on which to base such a diagnosis.

DR SAMUEL AYRES JR. My diagnosis is rosacea, probably of the gastrointestinal type. Was a tuberculin test performed?

DR MAX J WOLFF. My diagnosis is rosacea or lupus erythematosus.

DR JULIUS R SCHOLTZ. Although my conception of the clinical picture in this disease may be erroneous, I have made the diagnosis of a Lewandowsky tuberculid.

in 2 cases in which the clinical picture was exactly the same. They correspond to the case reported by Dr. Saul S. Robinson (*Urol. & Cutan. Rev.* 41:34, 1937). I agree with the diagnosis as presented. I was able to detect pinpoint brownish puncta on the forehead of this patient under diascopic pressure.

DR. SAUL S. ROBINSON: I consider the condition to be a rosacea-like tuberculid. Small brownish red papules, superimposed on an erythematous base, are scattered over the face. I suggest that if the disease does not respond to the treatment for ordinary rosacea the patient be given gold sodium thiosulfate, especially, if the tuberculin test gives a positive result.

DR. PAUL D. FOSTER: The reaction to a tuberculin test was slightly positive.

Lupus Erythematosus Involving the Tongue. Presented by Dr. C. RUSSELL ANDERSON.

Mrs. H. D., aged 40, was first seen in November 1938, because of painful erosion of the mouth and tongue of one year's duration and a facial eruption of one month's duration. Examination at that time showed leukoplakia-like striae and plaques on the dorsal surface of the tongue, with a superficial erosion on the right distal portion of the tongue. There was a similar erosion on the buccal mucosa of the right cheek. Retiform, white lesions resembling lichen planus were seen along the interdental line opposite the molar teeth. On the cheeks, the bridge of the nose and the midforehead were edematous red plaquelike lesions associated with mild scaling and follicular plugging. The cutaneous lesions were transitional between the chronic discoid and the subacute disseminated type of lupus erythematosus.

The dermatologic examination today shows two irregular superficial erosions on the sides of the tongue, with atrophy of the tip and the sides of the tongue. The leukoplakic appearance has largely disappeared. Serologic reactions were negative in November and December 1938 and in February 1939. The treatment has consisted of the administration of eleven intravenous injections of gold sodium thiosulfate from Nov. 10, 1938 to Jan. 18, 1939. This therapy resulted in the disappearance of the facial lesions, but no improvement of the stomatitis or glossitis was noted. On January 28 the buccal lesions were found to have become worse, and there was a slight recurrence of the facial lesions. The patient received azosulfamide (neoprontosil; disodium 4-sulfamidophenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene-3',6'-disulfonate), 10 grains (0.65 Gm.), four times a day. On the following day there was an acute flare-up of the facial lesion, with a universal lichenoid pruritic eruption. From January 29 to March 17 the patient received ten intravenous administrations of calcium gluconate, 10 cc. of a 10 per cent solution, and ten intramuscular injections of 100 mg. of bismuth subsalicylate. The cutaneous lesions entirely cleared, but the lesions of the mouth and the tongue showed no improvement.

DISCUSSION

DR. A. FLETCHER HALL JR.: I could not make a diagnosis of lupus erythematosus from the appearance of the tongue. The histologic section looks so much like some of the color slides that Dr. C. P. Rhodes showed in Philadelphia in November 1939, at the meeting of the American Academy of Dermatology and Syphilology, that I suggest treatment with vitamin B.

DR. WILLIAM GOECKERMAN: The condition does not now resemble lupus erythematosus of the tongue. It is puzzling that lesions as extensive as those in this case should disappear without atrophy.

DR. SAUL S. ROBINSON: I saw this patient in Dr. Anderson's office at the time that the cutaneous lesions were definite, and I agree with the diagnosis as presented.

DR. CHRIS HALLORAN: I do not believe that the lesions of the tongue are lupus erythematosus. I have never seen lesions of lupus erythematosus occurring in the buccal cavity, though it is not uncommon to see such lesions on the mucous

membranes of the lips The lesions on the tongue in this case impressed me as transitory benign plaques

A Case for Diagnosis (Pemphigus of the Eye? Fixed Eruption?) Presented by DR SAMUEL AYRES JR

Miss P B, aged 19, states that her left eye became "inflamed" about three and one-half years ago and has never entirely cleared The right eye has never been affected Cutaneous lesions in the right axilla and on the thighs have been present for about one and one-half years The patient believes that the ocular and the cutaneous lesions have synchronous periods of slight remission and exacerbation On several occasions during the past few months, the patient has taken sulfanilamide for as long as ten days, with some improvement She has also taken ex-lax in the past, but she denies the taking of any medicament containing phenolphthalein for the past six years There is no history of the presence of any foci of infection

The left eye shows severe inflammation, with redness that extends onto the face, considerable lacrimation and photophobia The conjunctiva is somewhat opaque, apparently owing to organization of the inflammatory process The right axilla and the medial aspect of each thigh present sharply defined, irregular, oval to circular, thickened violaceous plaques Microscopic examination of the cutaneous lesions for fungi on two occasions has given negative results

DISCUSSION

DR BEN NEWMAN (by invitation) Ocular pemphigus presents shrinking of the eyeball and folding of the conjunctiva These phenomena are not present here, and the condition is therefore not pemphigus

DR CHRIS HALLORAN I have under my care a patient with pemphigus vulgaris in whom the conjunctiva of one eye became temporarily involved There was no resultant shrinking of the eyeball during or following the conjunctival involvement

DR SAMUEL AYRES JR No definite diagnosis has been made The process is limited to the epithelial structure of the eye, according to the oculists In the only case of ocular pemphigus which I have observed blebs were present on the conjunctiva In this case I thought of a fixed eruption because of the lesions over the body

DR WILLIAM GOECKERMAN I have observed ocular pemphigus at the Mayo Clinic In none of the cases did true cutaneous pemphigus develop during years of observation I do not consider ocular pemphigus the same as true pemphigus, although bullae are not uncommonly seen on the conjunctiva

Oil Acne Presented by DR SAMUEL AYRES JR

O B B, a white man aged 24, has an extensive eruption that first appeared four or five months ago, while he was working in a plant which manufactures plumbing supplies The patient was in constant contact with "cutting oil," which saturated his arms and shirt, especially the sides of the trunk The eruption gradually increased in severity, and the patient stopped work about nineteen days ago There is no history of acne during adolescence

There is an extensive eruption, most severe on the arms and the sides of the trunk, but involving also the axillas, chest, abdomen and thighs The affected areas are studded with large comedos and show numerous papules, pustules and deep, fluctuant, abscess-like lesions The upper part of the back and the face are entirely free of lesions, except for a few comedos on the face

DISCUSSION

DR SAMUEL AYRES JR I have begun treatment with fractional doses of superficial roentgen radiation I have had no experience in treating oil acne with roentgen radiation, and I am wondering what type of response to expect

DR. WILLIAM GOECKERMAN: This is typical oil acne. I observed a simliar case in which a patch test with abrasive material to which the patient was exposed gave a positive reaction.

DR. H. C. L. LINDSAY: One should consider the occupational character of this disease and its relation to compensation.

DR. SAMUEL AYRES JR.: I consider this case to be one in which compensation should be made.

CHRIS R. HALLORAN, M.D., *Chairman*

SAUL S. ROBINSON, M.D., *Secretary*

April 9, 1940

Norwegian Scabies. Presented by DR. NELSON PAUL ANDERSON and DR. MILTON STOUT (by invitation).

D. B., a boy aged 13, has a history of having had "eczema" for variable lengths of time during infancy. About five years ago, "eczema" developed on the hands and soon spread to involve the trunk, legs, feet, head and neck. The patient has been in a number of hospitals for several weeks at a time and has attended many clinics, but no diagnosis of his eruption was made. There is a history of "skin trouble" in the mother and the grandmother. The patient was admitted to the Los Angeles County Hospital on March 13, 1940. He presents a generalized, scaling, moderately erythematous dermatitis. The soles, and the palms to a lesser degree, are covered with thick, greasy, gray crusts. The toe nails and finger nails are thickened and ridged. The right testicle is undescended.

Examination of the blood showed 85 per cent hemoglobin, 4,730,000 erythrocytes and 16,350 leukocytes, per cubic millimeter, 61.5 per cent polymorphnuclear neutrophils, 13 per cent lymphocytes, 4 per cent monocytes, 20.5 per cent eosinophils and 1 per cent basophils. The urine was normal. A roentgenogram of the chest showed slight prominence of the right hilar shadows, but the picture was not distinctive of tuberculosis. The histologic examination showed an irregular acanthotic epidermis, with moderate perivascular reaction in the upper part of the cutis. The histologic picture was somewhat psoriasiform, but was not that of true psoriasis.

DISCUSSION

DR. WILLIAM GOECKERMAN: I think the condition is ichthyosiform erythroderma.

DR. NELSON PAUL ANDERSON: I am sorry that there is no more discussion on this case. The condition is not pityriasis rubra pilaris. This is the first time in forty-two years that a case of this kind has been reported in this country. It is a typical case of Norwegian scabies. The condition was considered to be psoriasis, arsenical dermatitis or seborrheic dermatitis. The skin is loaded with scabies organisms. When certain changes took place recently, I took scrapings from one of the elbows, which revealed at least 20 acari of scabies. The changes in the nails are characteristic. The general erythematous dermatitis and the thickening of the palms and soles are also characteristic of this type of scabies. The organism is of the same type as that found in ordinary scabies. The first case, which occurred on Diseases of the Skin, ed. 5, Philadelphia, Lea & Febiger, 1937). For a time it was thought to be one of scabies of a type found only in lepers. The diagnosis in this case is correct, in my opinion. Therapy should be approached cautiously, as the patient will not tolerate vigorous treatment for scabies. This is the third

case to be reported in this country, the second case was reported in 1898. None of the authors of American textbooks claim to have seen a condition like it. It is transmitted actively, not passively. The man in the next bed is itching, and some of the nurses are complaining of the same trouble.

DR SAUL S. ROBINSON: I thought Norwegian scabies presented thick crusted lesions over the entire body.

DR NELSON PAUL ANDERSON: The patient had thick crusts when he came in. Another physician called the disease pityriasis rubra pilaris.

DR H. C. L. LINDSAY: I think the patient has ichthyosis scabies superimposed on ichthyosis. I have seen many patients who were supposed to have Norwegian scabies, but the diagnosis could not be proved.

DR KENDAL FROST: Dr. Anderson certainly deserves a word of compliment for making a brilliant diagnosis in a condition which few, if any, have ever seen.

DR WILLIAM GOECKERMAN: I should like further proof.

DR CHRIS HALIORAN: I request that the patient be presented again at the next meeting.

NOTE.—The patient was presented again one month later. The cutaneous lesions were greatly improved after treatment for scabies.

Primary Cutaneous Hodgkin's Disease Presented by DR H. C. L. LINDSAY and DR WALTER F. SCHWARTZ (by invitation)

Mrs. E. E. L., a Norwegian aged 66, has had facial paralysis and some numbness of the toes of the right foot for the past four years. For the past twelve years, she also has suffered from diabetes mellitus, which has been controlled for two years by protamine zinc insulin. About three and a half years ago a more or less generalized pruritic eruption developed, which has persisted and grown worse. The lesions begin as "little pustules" on an erythematous base and soon develop into firm nodules. There is no history of the ingestion of iodides or bromides. The generalized eruption is most prominent on the extensor surface of the hands, the forearms and the arms, as well as on the lateral aspects of the arms. The upper parts of the back, the chest, the buttocks and the thighs are also extensively affected. The eruption consists chiefly of excoriated, firm nodules and large papules. There are some lichenification and increased pigmentation in the parts chiefly affected. A few vesiculopustules are found in the center of bright erythematous patches, some of which measure nearly 1 cm. in diameter. These vesiculopustules represent early lesions. There is lymphadenopathy in the axillary and inguinal areas, some of the nodes being nearly 3 cm. in diameter. The spleen is barely palpable. The blood pressure is 180 systolic and 100 diastolic.

Examination of the blood showed 9,200 leukocytes per cubic millimeter, 70 per cent polymorphonuclear leukocytes, of which 16 per cent were stab cells and 54 per cent were segmented, 7 per cent monocytes, 5 per cent eosinophils, and 18 per cent lymphocytes. The urine showed no sugar.

Two specimens of tissue were taken for histologic study. The first area showed acute suppurative inflammation. In the other section there was no suppuration, but the cutis showed moderate edema, with perivascular inflammatory cell infiltration, including chiefly round cells, some plasma cells, occasional eosinophils and swollen fibroblasts and histiocytes. These cells were present about most of the blood vessels, down into the subcutaneous tissue. Occasionally between the nests of tumor tissue portions of the cutis showed swollen fibroblasts and a few eosinophils and round cells.

The treatment consisted of seven exposures of 80 r each to twenty-five fields.

DISCUSSION

DR IRVING R. BANCROFT: This case is not like the one at the Los Angeles County Hospital. It has different physical aspects.

DR SAMUEL AYRES, JR.: I consider the condition to be prurigo. To say that it is primary Hodgkin's disease means that there was no enlargement of the

lymph glands elsewhere, as in the mediastinum. The fact that the condition was present for two years without other involvement is against the diagnosis of Hodgkin's disease.

DR. JULIUS SCHOLTZ: This case impresses me as one of dermatitis herpetiformis. The lesions appeared in groups, and the location is fairly typical. Disappearing lesions have left pigmentation and atrophic scars. One would expect to find other signs of Hodgkin's disease in a condition of this duration. The histologic picture in this case is not definite enough to serve alone as the basis of the diagnosis.

DR. WILLIAM GOECKERMAN: I could see only excoriations due to the scratching. In a case of Hodgkin's disease the patient should have symptoms other than those of the skin. I saw nothing that would justify a diagnosis of dermatitis herpetiformis, and I do not think the microscopic picture warrants a diagnosis of Hodgkin's disease.

DR. WALTER F. SCHWARTZ (by invitation): I am not proud of my diagnosis. I saw a patient with a condition like this at a dermatologic meeting in Cleveland in 1938, and the diagnosis was Hodgkin's disease. The patient had had the cutaneous lesions fifteen years. Older lesions seemed nodular, some of which were closely grouped together. When I first saw this patient, she had many vesicles on an erythematous base. Eight biopsies were performed before the pathologic picture confirmed the diagnosis. I agree that it is not inconsistent with the findings in Hodgkin's disease. I am not sure of the diagnosis.

DR. SAMUEL AYRES JR.: What objection is there to the diagnosis of prurigo? DR. NELSON PAUL ANDERSON: I believe that this case is one of Hodgkin's disease of the skin. One of the sections can well be characterized as typical. I think Dr. Schwartz is correct in his diagnosis.

DR. L. F. X. WILHELM: I should like to see the patient again in six or eight months.

DR. H. C. L. LINDSAY: I thought at first that the disease was dermatitis herpetiformis, but not after I had seen the microscopic section. I have never encountered a case of prurigo in which there were so many lesions.

DR. WALTER SCHWARTZ (by invitation): I did consider the diagnosis of prurigo, but the onset was too late in life for this condition.

Naevus Linearis of the Arm; Lichen Acuminatus of the Legs. Presented by DR. IRVING R. BANCROFT.

E. H., a white man aged 50, complains of lesions on the right thumb, the little finger and the palm, which have been present since infancy. About thirty years ago a linear lesion appeared on the left arm. In 1915 similar lesions developed on the leg.

Dermatologic examination shows a patch of grouped papules on the left side of the chest. A linear papular eruption occurs on the left side of the chest and on the left arm. On the left leg are nodular lesions.

DISCUSSION

DR. A. FLETCHER HALL JR.: I thought the condition was linear lichen planus hypertrophicus.

DR. THOMAS W. NISBET, Pasadena, Calif.: I agree with the diagnosis as presented.

DR. KENDAL FROST: I agree with the diagnosis of nevus, although the condition could be linear hypertrophic lichen planus.

DR. FRANKLIN I. BALL: What is Dr. Bancroft's diagnosis? I agree that the condition is linear lichen planus of the hypertrophic type.

DR. L. F. X. WILHELM: I agree with the diagnosis. I think a biopsy should be done.

DR IRVING R BANCROFT The peculiarity of this lesion is that it appeared not at birth, but at the age of 6 or 7 years The lesions on the leg appeared at the age of 25 All the lesions were pruritic, particularly those on the leg

A Case for Diagnosis (Psoriasis? Eczema? Palmar Syphilid?) Presented by DR CLEMENT E COUNTER (by invitation), Long Beach, Calif

E S, a Portuguese aged 44, has had an eruption on the palms for two years The condition has become worse during the past four months On the palms and palmar surfaces of the fingers are dry, scaling lesions There are thickened areas on the knees and scaling patches on the scalp The serologic reaction of the blood has been strongly positive on two occasions during the past two weeks Microscopic examination of the scales for fungi gave negative results The urine was normal Treatment has consisted of one intramuscular injection of nonspecific protein and two fractional doses of roentgen radiation (75 r) No change has been noticed in the lesions as a result of this therapy

DISCUSSION

DR A FLETCHER HALL JR I thought this lesion was a late syphilid

DR BEN A NEWMAN (by invitation) I agree with the diagnosis of syphilid

DR SAMUEL AYRES JR I agree with the diagnosis of palmar syphilid

DR CLEMENT COUNTER (by invitation), Long Beach, Calif This lesion is interesting because it is bilateral and does not have a rolled edge to give it the appearance of a syphilid The history is misleading, because the area becomes much worse after manual labor I think the lesion will disappear with antisyphilitic treatment, but I believe that it is psoriasis

DR STANLEY C ANDERSON Because of the associated papular scaling lesions on the knees, elbows and scalp, I thought the condition was psoriasis of the palms

DR NELSON PAUL ANDERSON I agree with Dr Anderson

DR SAMUEL AYRES JR An interesting lesion on the man's wrist had the circinate appearance of syphilis There is a possibility that the man has two diseases

DR CHRIS HALLORAN I think this case should be presented again, for the results of pathologic examination are not yet available

Scleroderma Treated with Mecholyl Iontophoresis Presented by DR ANKER K JENSEN (by invitation)

V C, aged 15, was first examined on May 2, 1939 She complained of two lesions, one over the epigastrium and the other on the right breast, of two weeks' duration No subjective symptoms were associated with the eruption Examination now reveals two indurated oval areas, one on the right breast and the other beneath the breast The lesions have a pearly white, shiny center and a scarlet border The examination of the blood showed it to be normal The basal metabolic rate was +1 per cent The urine was normal Histologic examination showed dense collagenous bundles in the cutis, with chronic inflammatory infiltration about the sweat glands and the blood vessels Sixty-two treatments with mecholyl iontophoresis were given over forty-two weeks The results have been satisfactory

DISCUSSION

DR WILLIAM GOECKERMAN I think the condition is scleroderma To be a typical picture of scleroderma it should have had a more violaceous border This has probably been altered by the treatment

DR JOHN D ROGERS (by invitation) I saw this patient before she had had any treatment The lesion had an ivory appearance There has been decided improvement since treatment

DR THOMAS W NISBET, Pasadena, Calif I agree with the diagnosis

Keloid and Depressed Scars Subsequent to Ecthymatous Rupoid Syphilids. Presented by DR. IRVING R. BANCROFT and DR. O. M. STOUT (by invitation).

P. E., a woman aged 23, stated that she had had "chickenpox" in January 1939. The pustular lesions failed to heal, however, and new lesions continued to develop. Each treatment consisted of the removal of thick, rupoid crusts and the swabbing of the base of each lesion with hydrogen peroxide. On April 22 the patient was admitted to the Los Angeles County Hospital. She weighed 80 pounds (36 Kg.), and her general condition was poor. She presented generalized, fairly discrete, pustular, ecthymatous and rupial lesions, showing some scarring and evidence of healing. There were two necrotic ulcers on the soft palate and pharynx. The scalp was scarred and crusted. The serologic reaction of bismo-cymol, potassium iodide and neoarsphenamine. The response to treatment was good, but many keloids and depressed scars followed the disappearance of the rupial lesions.

DISCUSSION

DR. JULIUS R. SCHOLTZ: When this girl was in the ward, she showed widespread, heavily crusted, ulcerated lesions, a so-called malignant secondary syphilid, with extreme toxicity, high fever and prostration. She had lost more than 20 pounds (9 Kg.) in weight. Her response to treatment was prompt, and the scars became hypertrophic almost immediately. It is interesting to observe that some of the scars are at present thin and atrophic, while others show heavy keloids. I had another case similar to this; that of a young woman in whom secondary syphilis appeared five days after delivery. The course of the condition and the cutaneous lesions were practically identical with those of this patient.

DR. BEN A. NEWMAN: When the patient left the hospital all the scars were keloidal.

DR. SAMUEL AYRES JR.: This case is particularly interesting because of the fact that some of the keloids are linear. My first impression was that the disease was dermatitis factitia. I do not think, however, that there is any question as to the diagnosis now.

Pyoderma Faciale (O'Leary). Presented by DR. THOMAS W. NISBET, Pasadena, Calif.

R. W. S., a student aged 17, has a pustular eruption involving the face, of six months' duration. In November 1939 the lesions became rapidly worse and resulted in swelling and undermining by fluctuating abscesses. The patient suffered from general malaise, fever and loss of weight. Treatment consisted of the weekly administration of roentgen radiation (100 r), filtered through 0.5 mm. of aluminum, for three weeks and the local application of Danish ointment (an alkaline sulfur ointment). After each treatment there was an exacerbation of the eruption, with rupture of some of the abscesses. Shortly after the last treatment the condition began to subside rapidly, leaving deep keloidal scars.

DISCUSSION

DR. WILLIAM GOECKERMAN: I think this case is one of deep-seated acne.

DR. WALTER F. SCHWARTZ (by invitation): This is a new diagnostic term as far as I am concerned. I have been calling conditions like this acne conglobata.

DR. STANLEY C. ANDERSON: I call the condition severe pustular acne with keloids.

DR. SAMUEL AYRES JR.: I agree with Dr. Anderson.

DR. KENDAL FROST: I call the condition keloid developing in scars of acne conglobata.

DR THOMAS W NISBET, Pasadena, Calif This is the most acute acne I have ever seen The disease ran its course in one month I have never seen such swelling in a case of acne It is just like the pyoderma faciale described by Dr O'Leary

Onychomycosis Treated with Vaccine. Presented by DR HARRY P JACOBSON

Mr F S, aged 29, has had a fungous infection of the nails for seven years He believes that he contracted the infection from his wife, whose toe nails appeared to him to look like his own nails at the time of the first examination A variety of topical applications and a series of roentgen radiations administered during the past seven years afforded him no permanent relief At the time of the first examination the nails of all the toes, the left thumb and the index fingers were creamy yellow, disfigured and thickened The surfaces were exfoliating and striated Most of the involved nails were separated from their underlying beds, and the under surface of the nail plates were crumbly and irregular Scrapings from the under surface of the nails resulted in isolation from the toes of a pure culture of *Monilia* An unidentified hyphomycetic organism was recovered from the under surface of the left thumb nail Cutaneous testing with a filtrate of the culture of *Monilia* produced an erythematous, edematous, local reaction, 9 by 7 cm, which appeared several hours after the injection Vaccine therapy was started on Feb 19, 1940, with favorable results to date

DISCUSSION

DR ANKER K JENSEN (by invitation) I believe the treatment of fungous diseases with fungus vaccines is yet in the experimental stage One cannot be sure that some of the cures are due to their use Dr Lewis stated (Lewis, G M, and Hopper, M E An Introduction to Medical Mycology, Chicago, Year Book Publishers, Inc, 1939) that their use as a therapeutic agent is doubtful but that they are of value from a diagnostic standpoint

DR JULIUS SCHOLTZ I think the result is remarkable

DR SAMUEL AYRES JR I have not prepared vaccines by Dr Jacobson's method My vaccines have all been made by the carbon dioxide method I have not seen any beneficial results, although this failure may have been due to the preparation of the vaccines

DR A FLETCHER HALL JR When I saw this patient about two years ago, the condition did not look like a monilial infection There was a great deal of thickening of the toe nails and no friability The patient kept his nails thinned by constant filing parallel with the surface Whatever the cause, the result is excellent, and the patient shows an entirely different-looking set of nails than he did two years ago

Early Bilateral Blepharochalasis Presented by DR PAUL D FOSTER

I W, a white woman aged 25, complains of an eruption of the eyelids that began as a slightly reddened, edematous swelling of the upper and lower lids of both eyes The lesions have become more pronounced Examination of the blood showed a negative serologic reaction, 83 per cent hemoglobin, 4,500,000 erythrocytes per cubic millimeter, a color index of 0.92, 7,700 leukocytes per cubic millimeter, 39 per cent polymorphonuclear leukocytes, 53 per cent lymphocytes, 7 per cent monocytes and 1 per cent eosinophils The treatment has consisted of the application of roentgen radiation to the lids, with the use of the contact mercury shield and a mild emollient ointment

DISCUSSION

DR JULIUS SCHOLTZ This case corresponds closely to those described by Michelson and Laymon (Lichen Planus of the Eyelids, *ARCH DERMAT & SYPH* 37 27-29 [Jan] 1938 I have encountered 1 other case, that of Dr C Russell Anderson

DR. KENDAL FROST: Although the reticulum of the lesions in this case is much finer than that in the case to which Dr. Scholtz refers, there are certain similarities, and the condition in this case may be lichen planus of the eyelids. Incidentally, the early improvement in the other case did not continue. The last time I saw the patient she was not well.

A Case for Diagnosis (Granuloma Pyogenicum?). Presented by Dr. THOMAS W. NISBET, Pasadena, Calif.

D. M., a boy aged 7 months, has a lesion on the penis that appeared shortly after birth and lesions in the mouth and in the nose that appeared during the past three months.

The dermatologic examination shows a granulomatous lesion, the size of a large pea, on the frenum of the penis. A similar lesion is located in the left nostril, which is almost completely occluded by the growth. Two smaller lesions are present in the mouth: one on the anterior gingival margin of the lower jaw and the other on the inner surface of the left cheek.

A smear from the gingival lesion showed many large gram-positive cocci growing in pairs, tetrads and small clumps. Occasional gram-negative bacilli were also seen. No fungi could be found. The histologic examination of the lesion in the nose revealed granulomatous tissues. The Wassermann reaction of the blood and the results of dark field examinations were negative.

DISCUSSION

DR. KENDAL FROST: This case is one of the most interesting that has been presented for a long time. The two possible diagnoses which come to my mind are molluscum contagiosum and granuloma pyogenicum. The location is unusual for either.

DR. THOMAS W. NISBET, Pasadena, Calif.: I have no idea what the condition is. I thought of granuloma pyogenicum because, according to the history, the lesion bleeds easily.

DR. H. C. L. LINDSAY: I suggest the diagnosis of periadenitis mucosa necrotica. I encountered a case in which lesions such as these occurred in the mouth of a baby. There were also lesions in the mouths of the mother and the grandmother. The mother had similar lesions in the vagina. Those on the baby left scars.

CHRIS R. HALLORAN, M.D. *Chairman*

SAUL S. ROBINSON, M.D., *Secretary*

May 14, 1940

Lichen Planus of the Lips and Mouth. Presented by Dr. NELSON PAUL ANDERSON and Dr. O. M. STOUT (by invitation).

J. W., a Negress aged 37, complains of pigmentation of the lips of one and one-half years' duration. The discoloration has gradually increased and now affects the buccal mucous membranes. The Wassermann reaction of the blood was negative.

DISCUSSION

DR. KENDAL FROST: I have under my care at present a white woman with extensive lichen planus of the mouth and superficial erosions on the gums of the same type as in this case, a condition which I have never encountered heretofore. I also have never seen pigment on the mucous membranes in association with lichen planus, but that is probably a racial characteristic in Dr. Anderson's case.

DR SAMUEL AYRES JR I am not convinced of the diagnosis I feel that there is in one or two places, in addition to the appearance that suggests lichen planus, distinct evidence of gingivitis, with a certain amount of membrane formation Whether the gingivitis is a streptococcic or possibly a monilia infection I am not able to say I believe that the condition may be lichen planus plus something else I do not think one could say what the condition is with the amount of observation that has been given to the condition tonight

DR NELSON PAUL ANDERSON This case is a typical one of lichen planus The unusual feature is the amount of pigmentation that has occurred on the gums and buccal mucosa, and this is present while the lesions of lichen planus are in a state of activity

Multiple Benign Cystic Epithelioma Presented by DR NELSON PAUL ANDERSON

L C B, a white woman aged 32, has noted the slow development of multiple small nodules on the face during the past few years Scattered over the face are five or six solitary, split pea-sized, grayish white, cystic-appearing lesions The histologic examination showed the typical picture of benign cystic epithelioma

DISCUSSION

DR ANKER K JENSEN (by invitation) This case made me think how careful one has to be Surely, if I had seen the lesions on the face and not the microscopic section, I should have missed the diagnosis

DR NELSON PAUL ANDERSON I wish some one would tell me what to do for this condition besides making a diagnosis

DR SAUL S ROBINSON I had a patient a few years ago with a condition like this that was rather extensive along the nose and the upper lip Electrodesiccation and roentgen radiation were administered Smooth, flat scars resulted, and the patient was well pleased

Telangiectasia Following Infantile Eczema Presented by DR NELSON PAUL ANDERSON

S C M, a Mexican girl aged 5 years, presents numerous solitary dilated telangiectatic blood vessels in the center of both cheeks She had infantile eczema that began when she was 1 year old and persisted for about a year After the eczema cleared, the present condition was noted There is no history of any light treatments

DISCUSSION

DR JULIUS R SCHOLTZ I suggest a diagnosis of familial telangiectasia This patient shows telangiectasia not only of the cheeks but of the mucous membrane of the lower lip There is also a history that the girl's brother has frequent nosebleeds My impression is that the eczema probably is not related

DR L F X WILHELM I am inclined to agree with Dr Scholtz about the hereditary characteristics

DR NELSON PAUL ANDERSON I am not sure that this telangiectasia followed the eczema Sometimes one has to present a case with a questionable diagnosis in order to provoke a discussion Hereditary telangiectasia is eliminated, in the first place, by the symmetry of the eruption, and secondly, there is no family history of this disease I have seen both the father and the mother, and they are apparently normal I thought that the patient presented a striking picture I was prompted to present this case because physicians so often glibly tell the parent that when the eczema clears up the skin is going to be entirely normal

DR WALTER SCHWARTZ (by invitation) I noticed among persons I have recently examined that telangiectasia is rather common to men exposed to the

sun. I have also noticed that telangiectasia is common in those who are exposed to heat and to petroleum. Perhaps she had been out in the sun and telangiectasia resulted, provided it wasn't present before the eczema began.

DR. NELSON PAUL ANDERSON: The patient's brother, younger than she, has definite eczema.

A Case for Diagnosis (Boeck's Miliary Lupoid? Leprosy?). Presented by DR. A. FLETCHER HALL JR.

T. M., a Negro aged 20, complains that a nodule appeared on the right nasolabial fold one year ago. This lesion was followed within a few months by similar lesions in the corresponding location on the left side of the face and on the center of the cartilaginous portion of the nose. These lesions have broadened, and new nodules have developed, confluent with the original lesions. The central nasal lesion has broadened to form a plaque. The nodules occasionally become slightly inflamed for a few days but usually are inactive and asymptomatic. The patient believes that the nose has broadened during the past year. Examination shows a linear group of confluent noninflammatory nodules, each nodule being about 2 mm. in diameter, on each side of the nose, just proximal to the ala nasi. Across the broadest surface between these areas is a slightly elevated, sharply bordered, noninflammatory, oval smooth plaque. Comedos are scattered over the face. Several nodular lesions on the forehead resemble acne. The Eagle and Kline blood tests for syphilis gave negative reactions. Scrapings from the intranasal mucous membranes showed no acid-fast bacilli. The intradermal tuberculin test (with a dilution of 1 to 100) gave a negative reaction. The histologic section showed many acid-fast, gram-positive bacilli in the sebaceous ducts and orifices.

DISCUSSION

DR. MAX J. WOLFF: Clinically, I can see no evidence of leprosy in this patient. He has, on the other hand, lesions on the forehead and cheeks suggestive of acne.

DR. H. C. L. LINDSAY: I thought possibly the lesion on the nose was due to acne.

DR. NELSON PAUL ANDERSON: I am more or less responsible for asking Dr. Hall to present this case. Dr. Stout intended to present a patient from the Los Angeles County Hospital, one whom Dr. Frost will remember and whom Dr. Ormsby saw about a month ago. He is a Mexican boy with sarcoid-like lesions on both legs. Dr. Ormsby had no hesitation in making a clinical diagnosis of leprosy. The boy has a 4 plus Wassermann reaction of the blood. Strangely the lesions are rapidly responding to bismuth therapy. They are not the lesions of tertiary syphilis.

DR. A. FLETCHER HALL JR.: When I first saw this patient the clinical appearance suggested sarcoid. I took a specimen of tissue, sent it to the pathologist at the Santa Monica Hospital and asked for an acid-fast stain, as well as the usual hematoxylin and eosin stain. The pathologist told me there was a great number of acid-fast bacilli in bundles and thought the condition might be leprosy. When I looked at the section, I did see many acid-fast bacilli, but they were all in the ducts and orifices of the sebaceous glands. None were within the tissue proper. I do not know whether they are acid-fast or not; it seems to me that the smegma bacillus is acid-fast. The fact remains that there were a great number of acid-fast bacilli in the sebaceous orifices. The histologic picture does not resemble that of any disease in particular, unless possibly rhinophyma. I am at a loss to make a diagnosis. I do not believe this condition is acne because there is a definite plaque of a year's duration without inflammation. I should probably have not suggested leprosy as a possible diagnosis, because it is obvious that the section is in no way suggestive of that entity. I should like to know what the disease is—it is easy to tell what it isn't.

Leiomyoma Cutis Presented by DR SAUL S ROBINSON

Mrs L A G, aged 37, has had red nodules on the left forearm and back since early childhood. The patient states that the lesions contract and become tender and painful during cold weather.

The examination reveals multiple, discrete, pea-sized to cherry-sized, elevated, brownish red, firm nodules on the extensor surface of the left forearm and on the back. Some of the lesions are tender to touch.

DISCUSSION

DR KENDAL FROST I agree with the diagnosis, although I also believe that histologic confirmation is necessary. There is absence in this case of the lesion which I feel is probably the only characteristic gross one, namely, a coral pink globular papule, which is apparently the earliest lesion. Histologically these papules are solid, smooth muscle. At times a vermicular movement can be seen on their surface. In my case (*J A M A* 83 906 [Sept 20] 1924) the lightest touch to these lesions was followed by exquisite pain.

CHICAGO DERMATOLOGICAL SOCIETY

HERBERT RATTNER, M D, *President*

MICHAEL H EBERT, M D, *Secretary*

Feb 21, 1940

Naevus Unius Lateris (Angiomatous) Presented by DR EARLE R PACE (by invitation)

A blonde girl aged 2 years and 3 months is presented from the dermatologic department of the Research and Educational Hospital, University of Illinois. She has a handlike angiomatous eruption of the right lower extremity, which was first noted at the age of 1 year and 2 months. It extends from the lower part of the right buttock downward in an irregularly widening strip over the thigh and leg to the shoe top. On the leg it occupies almost the entire lateral half of the surface. It consists of small pinhead-sized to pea-sized flat-topped red papules, irregularly grouped. Vitopressure removes all the redness and reveals depigmentation of the overlying epidermis. Most of the papules seem purely angiomatous, but a few have a slight follicular keratotic element. The condition is asymptomatic. There are questionable residues of somewhat similar lesions on the right arm. The mother states that there was a lesion on the left side of the lower lip earlier in life, which had been considered a "birthmark."

DISCUSSION

DR L M WIEDER, Milwaukee I agree with the diagnosis. I suggest treatment with solid carbon dioxide.

DR M H EBERT I wonder if this case might not be one of angiooma serpiginosum. The lesions are of the type that is described in that disease. They are somewhat annular. It would be interesting to know if there were any absorption of the old lesions and progression of new ones.

DR EARLE R PACE (by invitation) I cannot answer Dr Ebert's question because I have had the case under observation for only three or four weeks.

Pseudoxanthoma Elasticum Presented by DR OLIVER S ORMSBY

In this boy aged 14 the condition has been present for twelve years. The first change was noticed around the umbilicus when he was 2 years old. The lesions

spread peripherally and cleared centrally, according to the recollection of the patient's mother. New lesions have developed on the sides of the neck during the last six months. At present there is a diffuse eruption on the abdomen except for a palm-sized area in the center which is now clear. The eruption is also present on the sides of the neck. The primary lesion is apparently a match head-sized flat papule, slightly elevated, presenting a yellowish tinge. On diascopic pressure the yellow tinge becomes more evident. There are no subjective symptoms.

The histologic changes described by Dr. Ebert are as follows: In the sections stained with hematoxylin and eosin, the principal change was seen in the midcorium. In a large oval area the collagen bundles were smaller than normal and compressed by numerous small, amorphous, basophilic masses. The elastic tissue was stained with Weigert's stain. In the affected area it was fragmented. Some of the elastic fibers were swollen and transversely jointed. There were also many small, irregular pale-staining amorphous masses.

No striae were detected in the choroids by Dr. Von der Heydt. He did report a mottled condition in the choroid in the right eye, however, together with a few peculiar choroidal dots on the left. The examination was not completely satisfactory, because it was not possible to use a mydriatic.

DISCUSSION

DR. F. E. SENEAR: The lesions on the sides of the neck were characteristic, but I do not recall having seen pseudoxanthoma elasticum on the abdominal region before, and I probably should not have thought of that diagnosis had the disorder not been present on the neck also.

DR. C. W. FINNERUD: I did not see the patient, but I saw the sections. On first glance the condition appeared definitely to be pseudoxanthoma elasticum. The greater part of the change is in the collagenous tissue, much more than in the elastica. Many of the elastic fibers in the involved area are of normal appearance.

DR. M. R. CARO: The changes in the elastic fibers are not as pronounced as those ordinarily seen in pseudoxanthoma elasticum, but I thought that the section was compatible with that diagnosis.

DR. OLIVER S. ORMSBY: I had hoped that the condition in this case would prove to be an early sclerodermoid nevus. I reported such a case about three years ago (Ormsby, O. S.: *Diseases of the Skin*, Philadelphia, Lea & Febiger, 1937, ed. 5, p. 536), and no others have been observed. When tissue was excised in the present case it resisted the knife as though there were sclerotic changes, but the histologic sections definitely ruled out a nevus. The only condition in which changes in the elastic tissue such as the present ones are found is pseudoxanthoma elasticum.

DR. M. H. EBERT: In regard to the histologic sections, I do not believe that with the use of the Weigert stain the discoloration was complete, which was a little confusing. There were many amorphous masses throughout the section, which I interpreted as degenerated elastic tissue. I thought that some of them perhaps had been calcified. In the literature on this disease, the term "naevus elasticus" has been suggested, as Dr. Finnerud knows. I think the term might well apply in this case.

DR. OLIVER S. ORMSBY: This condition is rare. I doubt if any one here has encountered more than 3 or 4 cases. There may be changes in some of the cases that are not classic, yet they represent the same disease. I am glad to hear Dr. Finnerud state that the disease resembles pseudoxanthoma elasticum more than any other disease, though it is not classic.

I think the ocular changes are important because, while striae were not demonstrable with the hasty examination, I think they will be when a mydriatic is used and the retina is properly shown. The mottling found there was characteristic of what is seen in pseudoxanthoma elasticum.

A Case for Diagnosis (Mycosis Fungoides?). Presented by DR F E SENEAR and DR F J KENDRICK (by invitation), Gary, Ind

Mrs W, aged 35, was seen in June 1938, at which time she presented a generalized bullous eruption due to barbiturate-sunlight sensitization, which subsided with ordinary treatment. Six months later she was seen with an eruption on the back of the neck, the breasts and the left forearm consisting of grouped, flat, violaceous, papular lesions more or less polycyclically arranged. The results of histologic examination were not conclusive, but lichen planus was considered as a possible diagnosis. Most of the lesions cleared up by treatment with a bismuth compound intramuscularly and roentgen rays locally. Four months ago the patient was seen again with nondescript eczematoid patches chiefly on the arms and neck.

Now the patient presents slightly infiltrated, somewhat configurated, dull-colored eczematoid patches on the dorsa of the forearms and on the right side of the neck. I have considered parapsoriasis, mycosis fungoides and lupus erythematosus as possible diagnoses. A histologic section is shown.

Mycosis Fungoides (Prefungoid Stage) Presented by DR F E SENEAR and DR F J KENDRICK (by invitation), Gary, Ind

Mrs B, aged 45, has had generalized pruritus accompanied by an eruption for fifteen years. Lately the itching has been more persistent and the eruption, instead of fading periodically, has become more pronounced.

Examination reveals polycyclic, annular, margined, slightly scaly, slightly infiltrated patches on the inner aspects of the thighs and calves, in both groins and in a smaller area on the chest. The eruption was much more pronounced ten days ago, before the administration of $\frac{1}{4}$ unit of roentgen rays to the involved areas. Serologic reactions were negative. A histologic section is shown.

DISCUSSION OF CASES OF MYCOSIS FUNGOIDES

DR H R FOERSTER, Milwaukee. These 2 cases are rather difficult to discuss because neither eruption showed a clear picture of the condition suggested for diagnosis. In the first patient the lesions on the forearms showed none of the characteristics of lupus erythematosus. The morphologic changes and distribution suggested a toxic erythema of the multiforme type, with the possibility of photosensitivity having caused the lesions to be localized on exposed surfaces. This possibility is also suggested by the history that last summer she had an actinic dermatitis which was apparently more than a sunburn following the ingestion of a barbiturate and exposure to sunlight. The lesions did not suggest lichen planus to me, but I have seen lichenoid eruptions in cases of actinic dermatitis.

The second patient may have early mycosis fungoides of the prefungoid type, as suggested by the history and distribution and configuration of the lesions and by the histologic section, but the disease has apparently not developed to the stage at which one can state with certainty that it is more than that type of dermatitis.

DR F E SENEAR. I saw the first patient several days ago and was unable to come to any conclusion as to the diagnosis. I thought of psoriasis and parapsoriasis, in addition to several conditions that Dr Foerster suggested. I do not think the case is one of classic mycosis fungoides.

DR L F WEBER. In the first case I suggest as a diagnosis the condition described by both Cannon and Sulzberger, allergic dermatitis simulating lymphoblastoma. While the eruption today does not fit in with that possibility, I think there is a likelihood that it may do so some time later.

Syringocystoma Confined to the Face DR L F WEBER

Mrs M McK, an American woman aged 39, for the past fifteen years has had an eruption of the cheeks, nose and eyelids. The lesions are from 1 to 4 mm

in diameter. They are round, smooth papules and nodules. Many are discrete and a few are closely aggregated. They are soft. The color is yellowish; some lesions are lighter than others, and a few have a waxy appearance. Slight itching is present at times. The histologic diagnosis was syringocystoma.

DISCUSSION

DR. J. H. MITCHELL: I should like to suggest the use of the spark. I often treat similar lesions with this method, with satisfactory results.

DR. L. F. WEBER: My object was to show that the eruption was limited to the face. Usually one would expect to find lesions on the chest and back. I am grateful to Dr. Mitchell for his therapeutic suggestion.

Lupus Erythematosus. Presented by DR. HERBERT RATTNER and DR. IRENE NEUHAUSER (by invitation).

E. B., a white woman aged 62, states that nine years ago her eyes became red, slightly painful and sensitive to light, and this condition was accompanied by lacrimation. About one month later redness developed on the eyelids, which she attributed to the drops used in her eyes. At that time a diagnosis was made of conjunctivitis of unknown origin and dermatitis. Since that time she has had frequent recurrences of ocular symptoms and exacerbations of the lesions on the face, which have never completely cleared up. She has never noticed any seasonal changes but thinks the condition is made worse by ultraviolet irradiation, which she is receiving for the eyes.

She presents superficial, slightly infiltrated, erythematous lesions on the lower eyelids. The lesions have a fairly well defined border and are scantily covered with scales. Some patches are puffy in appearance, with little tendency toward scaliness and little evidence of atrophy. There are some ill defined, superficial patches in the nasolabial fold, on the tip of the nose and on the mucocutaneous border of the lips.

Recent examination of the eyes by an ophthalmologist showed edema of the conjunctiva, with scarring.

Histologic examination showed a thin parakeratotic scale. The epidermis was thinned and showed considerable intracellular edema. In one place a small vesicle was present. The upper part of the corium showed edema and degeneration of the collagen and elastic fibers. The blood vessels were dilated and were surrounded by loose mantles of lymphocytes and a few histiocytes.

DISCUSSION

DR. L. F. WEBER: When I looked at that patient I was impressed that she probably had contact dermatitis, but after looking at the section I agree with the presenters' diagnosis.

DR. F. E. SENEAR: I saw this patient several days ago, and today was struck by the change in the clinical appearance since then. I am still of the opinion that the condition is lupus erythematosus. I do not think many physicians have seen many patients with lupus erythematosus involving the eyes. It is interesting that the ocular picture today is more like that which occurs in association with rosacea. I do not mean to suggest that the disease present is rosacea, but the ocular changes are not those which are usually seen on the conjunctivas of patients with lupus erythematosus.

DR. OLIVER S. ORMSBY: Do you think the ultraviolet irradiation aggravated the condition?

DR. IRENE NEUHAUSER (by invitation): We have been watching the patient for several weeks, and the picture changes each time we see her. The ultraviolet irradiation for the eyes may be responsible for some of the changes, but it does not seem to make the condition worse.

DR OLIVER S ORMSBY In my experience sunburn is hazardous in cases of lupus erythematosus. Recently I saw a patient who succumbed to acute disseminated lupus erythematosus which was precipitated last summer by sunburn.

DR M R CARO The histologic picture is compatible with that of lupus erythematosus. There is a small vesicle in the epidermis which is not ordinarily seen in lupus erythematosus, but this may have been produced by some external agent.

DR C W FINNERUD Dr Kren (*Arch f Dermat u Syph* 83 13, 1907), in describing lesions of lupus erythematosus of the mouth and mucous membrane elsewhere, described involvement of the conjunctiva in the chronic discoid variety. Such involvement was also described by Klauder and DeLong (*Arch Ophth* 7 856 [June] 1932).

DR M H EBERT Dr Rattner will remember a Negro in the Cook County Hospital who had extensive lupus erythematosus with involvement of the conjunctivas. He was treated with injections of bismuth compound, and the ocular lesions responded rapidly. I think the condition in this case is lupus erythematosus of the conjunctiva.

Scleroderma (Diffuse and Circumscribed) Presented by DR T BENEDEK (by invitation)

Xanthomatosis Presented by DR M H EBERT

Mrs M K, a white woman aged 36, complains of yellowish nodules on the fingers, jaundice and pruritus. On about April 1, 1939 she noticed that the skin turned yellowish overnight. There was no pain, itching was moderate. There was fulness after meals, with relief by regurgitation and elimination of gas. Various diets failed to relieve any of the symptoms. She was admitted to the Cook County Hospital in June 1939, where on operation a gland was removed from a site adjacent to the common duct. Up to this time she had lost 32 pounds (14.5 Kg) in weight. She was readmitted in November 1939 for a check-up, with the jaundice, itching, bloating and belching still present. While in the hospital she first noticed the formation of yellowish "calluses" on the fingers. There has been a progressive enlargement of these up to the present time.

Examination reveals a moderate icterus of the skin and scleras. The skin appears dry and lichenified and shows excoriations. On both legs are small crusted papules. No oral lesions are demonstrable. The liver is 3 fingerbreadths below the costal margin. The spleen is not palpable. On the flexural creases of the fingers are linear hard waxy yellowish nodules raised about 2 mm from the surface of the skin. These are slightly tender. On the lower right lid at the outer canthus of the eye is a small, yellowish, split pea-sized plaque. On eversion of the lower lid this plaque is seen to be merely an extension of a xanthomatous nodule situated on the conjunctival border of the lower lid.

The gland removed at operation in June showed benign hyperplasia. In November the icteric index was 75 and the cholesterol content of the blood 1,000 mg per hundred cubic centimeters, with 533 mg cholesterol esters. Three weeks ago the icteric index was 93.6 and the cholesterol content 1,100 mg, with cholesterol esters 889 mg. At present the cholesterol amounts to 1,288 mg, with cholesterol esters 1,100 mg, the phosphorus to 925 mg (normal 4 mg), the phosphatase to 79.15 units (normal 3 units) and total lipoids to 533 mg per hundred cubic centimeters.

In November 1939 roentgenograms of the esophagus, chest and abdomen were normal except for the nonvisualization of the gallbladder.

Tissue from the flexor surface of the finger fixed in solution of formaldehyde was studied histologically. All sections were frozen, and a hematoxylin-eosin stain was used. There were many groups of large cells, with typical foamy

cytoplasm in the upper part of the corium and a few Touton gram cells. There were marked hyperkeratosis and parakeratosis. When stained with sudan III, the foam cells were seen to be packed with lipoid granules and crystals. Lipoid material was found in some of the intercellular spaces of the rete mucosa.

DISCUSSION

DR. M. H. EBERT: Obstructive jaundice, whether the cause is a malignant condition or not, results in hyperlipemia and not so much in hypercholesteremia. In this case both the cholesterol esters and the total lipids were greatly increased. Our chemical studies have been limited to what could be done at the hospital. In all cases of obstructive jaundice there is an increase in the lipids, but xanthoma does not develop in all of them. In a large percentage of cases xanthoma occurs at the site of pressure on the fingers and hands.

Bowen's Disease. Presented by DR. THEODORE CORNBLEET and DR. H. C. SCHORR (by invitation).

M. D., a Negress aged 54, three years ago noted a small bean-sized lump under the left axilla. This broke down and left a small ulcerating surface which spread gradually by peripheral extension until it reached the present size. Itching has been marked. The patient has been treating the condition by washing it with solution of boric acid and then applying a phenol ointment.

Examination shows a large superficially ulcerating lesion extending across the entire axillary fold on the left side. It extends down the thorax about 3 inches (7.5 cm.) in semicircular fashion and down the medial surface of the arm in like manner for approximately 1 inch (2.5 cm.). The center portion shows an eroded surface with a grayish white membrane covering various parts in a bizarre pattern. The borders are scalloped and show increased pigmentation.

The results of Kahn and Wassermann tests were negative. There were no fungi on direct smear or culture.

Histologic examination of a section of skin revealed a portion of relatively normal skin with a thin stratum corneum and a slight acanthosis of the rete pegs. Adjacent to the normal skin the stratum corneum was missing and replaced by a necrotic membrane infiltrated by many polymorphonuclear leukocytes. The stratum granulosum was likewise missing, but the rete pegs showed decided acanthosis. The cells in the rete layer were large. The nuclei in places were irregular, and atypical mitotic figures were seen. Many of the nuclei contained distinct nucleoli. The line of demarcation between the rete pegs and the papillary layer was distinct. The papillary layer was heavily infiltrated by numerous lymphocytes. This picture is compatible with a diagnosis of Bowen's disease.

DISCUSSION

DR. L. M. WIEDER, Milwaukee: I think the border of the lesion posteriorly would suggest clinically a superficial basal cell lesion. The histologic diagnosis, however, showed that the condition was not that disease.

Pityriasis Rubra Pilaris. Presented by DR. DAVID V. OMENS and DR. WALTER W. TOBIN (by invitation).

The mother of this child (R. C., aged 2 years and 3 months) states that three weeks after birth the child's hands and feet became reddened as though sunburned, and then scaly and roughened. Within a month the whole body became similarly involved. The child scratches almost constantly. Treatment with external applications has not helped.

The family history is essentially normal. There are no other children in the family.

The child presents an almost universal dry, scaling erythematous dermatitis which involves especially the hands and feet, forearms and legs, lumbar area and nucha. The hyperkeratosis and pinhead-sized follicular papules give the appearance of gooseflesh. The palms and soles are lemon yellow.

The urinalysis and the blood count gave negative results. A tuberculin test, with 0.1 cc of 1:1,000 solution, gave a negative result.

DISCUSSION

DR J. H. MITCHELL: I presented this case in the clinic as one of probable pityriasis rubra pilaris. I think the diagnosis was correct.

DR M. OPPENHEIM (by invitation): There is no doubt that the child shows lichen rubra acuminatus or pityriasis rubra pilaris (Devergie's disease), which the Viennese school identifies as the same. There is only one other diagnosis that might come into consideration and which is the second form of congenital ichthyosis, erythroderma exfoliativum congenitum. But in this case that diagnosis can be excluded, because the skin shows normal areas, which are never found in ichthyosis congenita.

Leprosy Presented by DR M. H. EBERT and DR DAVID V. OMENS

Kaposi's Sarcoma Presented by DR HERBERT RATTNER and DR IRLNE NEUHAUSER (by invitation)

J. Y., a laborer aged 59, born in Yugoslavia, first noticed a lesion on the right thenar eminence four or five years ago, followed by the development of a small lesion on the right lower extremity, which gradually became larger. New lesions have appeared from time to time on the extremities and on the left buttock. To the patient's knowledge, none of the lesions has disappeared spontaneously. He came to the clinic because of swelling and a feeling of heaviness of the lower extremities. He has had no other objective symptoms.

Examination reveals a firm, sharply defined, raised, infiltrated, bluish red triangular-shaped plaque on the anterior surface of the lower third of the right leg. On the upper and lower extremities and on the left buttock are similar bluish red lesions varying in size from that of a pea to that of a silver dollar. Some lesions have coalesced to form diffuse, ill defined infiltrations. There is some swelling of a boardlike character involving both feet and ankles. The liver is palpable, the inguinal glands are enlarged and firm.

The Kahn reaction was negative. A blood count revealed 96 per cent hemoglobin and 4,660,000 erythrocytes and 7,500 leukocytes per cubic millimeter, with a differential count of 71 per cent neutrophils, 21 per cent lymphocytes, 2 per cent eosinophils, 1 per cent basophils and 5 per cent monocytes. A roentgenogram of the chest and pelvic bones was normal. The nonprotein nitrogen of the blood amounted to 36 mg, the creatinine to 1.9 mg and the sugar to 79 mg per hundred cubic centimeters. Sternal puncture showed essentially normal bone marrow, with some evidence of nonspecific irritation.

Histologic examination of tissue taken from the leg showed the epidermis to be flattened. The upper part of the corium was edematous. Throughout the corium were many newly formed blood vessels surrounded by a diffuse cellular infiltration and by many brown pigment granules. These were shown to be iron pigment by Perle's prussian blue reaction.

DISCUSSION

DR M. H. EBERT: I took a specimen recently from an early lesion in this patient, which showed a decided deposition of hemosiderin, proliferation of the blood vessels and changes in the perivascular connective tissue characteristic of Kaposi's sarcoma.

Juxta-Articular Nodes; Syphilis. Presented by Dr. S. J. ZAKON (by invitation). R. K., an American man aged 32, first noted the appearance of hard, painless growths on his palms seven years ago. These have been increasing in number and in size, and in the last two years he also has noted similar growths on his elbows.

Examination on Jan. 6, 1940 revealed the presence of hard, nontender, subcutaneous, symmetrically distributed, polylobulated nodes on both forearms about 5 cm. distal to the olecranon process. There were two nodes on each elbow. On both palms there were many (eighteen on each) hard, painless nodes and nodules, varying in size from a few millimeters to 2 cm. They were covered with hyperkeratotic skin and seemed to be attached to the overlying skin. None of the lesions bore any relation to the bursa. The Wassermann and Kahn reactions were strongly positive. One node was removed from the left elbow for histologic study. The patient has received iodides and six injections of a bismuth compound thus far, and there is a definite diminution in the size of the growths.

DISCUSSION

Dr. A. W. STILLIANS: This is the first case in which I have seen lesions on the palms. I understand they are not common.

Dr. J. H. MITCHELL: This is the second case in which I have seen such large and numerous lesions on the palms. Dr. Ormsby's case was the first.

Pemphigus Vulgaris. Presented by Dr. THEODORE CORNBLEET and Dr. HERBERT RATTNER.

J. G., a white Polish man aged 64, presents a bullous eruption. He states that about four weeks ago he noticed tenderness of the tongue. One week later blisters appeared in his mouth, the right axilla and the right groin and on the toes of both feet simultaneously. Despite treatment by his physician for eczematoid ringworm of the toes, the condition has grown progressively worse. He denies having had previous attacks and states that he has been well all his life. His family history is irrelevant.

Examination of the mouth reveals numerous erosions of the tongue and buccal mucosa circumscribed by overhanging white epithelium. The lesions give off an offensive sweetish odor. The right axilla presents a walnut-sized crusted nodule which also emits this offensive odor. Present in the fold of the right inguinal region are several infiltrated elongated masses covered with vesicles, bullae and macerated skin.

In both cubital areas and on the buttocks are erythematous, edematous, raw and empty bullae, with the epithelium which covered the bullae hanging loose. The back presents a pinkish maculopapular eruption. All of the toes are acutely inflamed and edematous, while the interdigital spaces reveal denuded bleeding surfaces partially covered with necrotic grayish white epithelium. Nikolsky's sign cannot be elicited.

In the past five days the oral cavity has become less tender and the lesions have healed, especially those on the tongue. Also there has been some improvement of the toes and other areas involved. The patient has been taking sulapyridine, one tablet four times a day for the past three days. Since admission his temperature has ranged from normal to 100 F.

The urine was normal. A blood count showed 102 per cent hemoglobin and 5,970,000 erythrocytes and 13,950 leukocytes per hundred cubic centimeters, with a differential count of 67 per cent neutrophils, 15 per cent eosinophils, 2 per cent basophils, 15 per cent lymphocytes, 1 per cent monocytes and microcytosis. The fasting blood sugar value was 93 mg. per hundred cubic centimeters. A Kahn reaction of the blood was negative. The nonprotein nitrogen content of the blood was 49 mg. and the uric acid content 4.6 mg. per hundred cubic centimeters.

Pemphigus Presented by DR THEODORE CORNBLEET and DR HERBERT RATTNER

A A, a man aged 73, born in Scotland, was presented at the last meeting of the Chicago Dermatological Society (ARCH DERMAT & SYPH, to be published), with a bullous eruption of the areas usually involved in Duhring's disease. Since then he has had almost a daily eruption of new vesicles and bullae either on the upper or on the lower extremities, with healing of the older lesions. He had a slight elevation of temperature, ranging from normal to 100 F, until February 15, when he was given sulfapyridine, one tablet four times a day, since that time his temperature has not risen above 99 F. New vesicles and bullae have developed since he has been taking sulfapyridine, but not as many or as tense ones as previously. Also his general condition has improved.

DISCUSSION OF CASES OF PEMPHIGUS

DR M R CARO I have had no experience with sulfapyridine in the treatment of pemphigus. The treatment of pemphigus with sulfanilamide has not been entirely satisfactory. The 2 patients I treated originally are both dead. The man died of a cardiac complication and the woman of a pulmonary infarct from an infected bed sore. The skin of the latter patient was entirely clear until the day before death, when a profuse generalized vesicular eruption appeared.

DR F E SENEAR It might be interesting to report on the child I showed last month (ARCH DERMAT & SYPH 42:198 [July] 1940). The eruption was generally thought to be dermatitis herpetiformis. I believe Dr Parkhurst said that sulfanilamide had been used, without effect. A member of the pediatric department gave the child sulfapyridine with rapid improvement. Treatment was stopped for a week, during which the condition recurred. With resumption of the sulfapyridine therapy, the child showed rapid improvement. This cannot as yet be accepted as conclusive evidence that sulfapyridine was responsible for the improvement.

DR HERBERT RATTNER There is an interesting case at Michael Reese Hospital, that of a man treated with sulfanilamide for disease of the middle ear and then discharged as cured. He reentered the hospital after a week with the picture of exfoliative dermatitis, presumably from the sulfanilamide. He now has pemphigus foliaceus.

DR OLIVER S ORMSBY Concerning sulfanilamide in the treatment of pemphigus, I might say I have not had good results with it. I have had a patient under observation for eighteen years who had severe erythema multiforme. Each attack has lasted three or four months. Some of the time the lesions resembled a streptococcal infection, and at other times, Vincent's angina. Until four years ago the attacks were of such severity that he could not carry on work of any moment. His former attacks yielded best to arsphenamine. For four years he was comparatively free. About the middle of January he entered the hospital with the first attack he had had in four years, and his condition was serious. He was toxic and had a high temperature, and his mouth presented the appearance of a streptococcal infection. The mucosa of mouth, tongue, gums, pharynx, larynx and trachea was gone in some areas and covered with gray pellicles in other places. Swallowing was difficult. He also had other symptoms of erythema multiforme on the skin of the extremities. He was hospitalized and given sulfanilamide, and in two weeks his skin was entirely cleared. He was kept under treatment for another ten days. I believe the basis of his multiform erythema was an infection. The disease in his case was severe and resistant to treatment until the last attack.

DR THEODORE CORNBLEET The use of sulfanilamide in Duhring's disease was called to my attention by statements in the literature, as well as by its favorable effect on the patient of whom Dr Senear spoke at last month's meeting. The first case was presented as one of possible pemphigus. I think there is some question about that diagnosis. It is possible that this patient has erythema multiforme. The eruption started in the mouth and then extended down to the toes.

where it was thought to be an acute eczematoid ringworm. The man was losing ground. In my opinion he shows decided improvement, especially of the mouth, since he was given sulfapyridine. He is as yet by no means on the way to complete relief, but I think it is well to record here that there is some progress in his case.

The man with dermatitis herpetiformis has also shown decided improvement with the use of sulfapyridine. It is true he showed some improvement before its use, but it seems to me that the improvement has been accelerated with the use of sulfapyridine.

Epidermolysis Bullosa Acquisita. Presented by DR. JAMES H. MITCHELL and DR. WALTER W. TOBIN (by invitation).

This girl, aged 13, states that approximately five years ago blisters began to appear on her hands, feet, elbows and knees, which caused little distress but left scars on healing. The blisters seemed to come in attacks at irregular intervals. There is no familial history of any similar eruption.

Examination discloses dusky erythematous patches of the hands and feet, with noninflammatory bullae about the fingertips and the toes. There are also whitish atrophic areas on the dorsa of the hands as well as over the elbows and knees. Examination of the urine and the blood gave negative results. The reaction to 0.1 cc. of a 1:10,000 dilution of tuberculin was negative. Histologic examination of the tissue taken from an active lesion showed acanthosis, with a large vesicle in the epidermis. The cutis was practically unchanged except for a reduction of elastic tissue.

DISCUSSION

DR. F. W. LYNCH, St. Paul: An interesting family history was obtained from 2 children whom I saw a few days ago with severe dystrophic epidermolysis bullosa. The parents are first cousins and have four children. The first and fourth are boys and have the disease mentioned. The second and third are girls and present no evidence of this disease. This history suggests that congenital dystrophic epidermolysis bullosa is transmitted as a recessive characteristic, as has been noted on numerous occasions. Sex linkage is also evident.

DR. JAMES H. MITCHELL: Dr. Tobin and I have discussed this case at some length, but I cannot satisfy myself that the diagnosis is correct. I do not know what it is.

DR. WALTER W. TOBIN (by invitation): I think the condition is a typical acquired form of dystrophia bullosa. The scars in association with vesicular and bullous lesions and the histologic picture would tend to prove that, because of the bullae in the epidermis with practically no infiltrate about them. There was some question of a vasomotor disorder being responsible since the condition is apparently a mild form.

A Case for Diagnosis (Psoriasis? Pityriasis Rubra Pilaris?). Presented by DR. M. H. EBERT.

V. M., a 17 year old Negro, presents a generalized follicular eruption. He states that he never had any disease of the skin except some sores on his scalp about three years ago, which healed in a few weeks with the application of a salve. His present eruption began about five weeks ago, as a scaly patch on the left thigh. Three weeks ago, all over the body and the extremities there developed small bumps, like "goose flesh," which itched moderately. The face and scalp became scaly at about the same time.

There is no history of any similar trouble or of tuberculosis in the family. The patient also states that he has not eaten fresh vegetables or fruits oftener than once or twice in two weeks.

Examination of the urine gave negative results. A Kahn reaction of the blood was negative. A blood count showed 86 per cent hemoglobin and 4,260,000 erythro-

cytes and 8,400 leukocytes per cubic millimeter, with a differential count of 55 per cent neutrophils, 2 per cent eosinophils, 3 per cent basophils, 25 per cent lymphocytes and 5 per cent monocytes, an occasional immature cell of the lymphocytic series was seen. The basal metabolic rate was — 9 per cent. The ascorbic acid content of the blood was 0.025 mg per hundred cubic centimeters (normal, 0.74 to 1.38 mg).

The physical examination gave negative results. The skin of the scalp, ears and face is covered with fine, firmly adherent scales. The lower lids are injected and drawn slightly down and outward. The neck, the extensor surfaces of the extremities, including the dorsa of the hands, and the sides of the trunk present mildly inflammatory acuminate firm papules situated at the mouth of follicles, and at the apex, a horny plug or scale which dips into the follicle. In the hairy areas a hair protrudes from the center of the papule. Some of the tops of the papules have been excoriated. On the thighs and elbows are a few variously sized and shaped flat plaques covered with a silvery scale. The skin of the palms is thickened. There is a generalized adenopathy.

Examination of the eyes showed the conjunctivas to be decidedly injected and granular, without the normal shining appearance, there was a faint tinge of yellow, suggestive of xerosis.

A roentgenogram of the lungs disclosed an increase of the hilar markings, with a small amount of fibrotic infiltration extending into the parenchyma, early tuberculosis was not ruled out, but the picture was not typical.

Histologic study revealed a decided thickening of the parakeratotic stratum corneum, the stratum granulosum in places was well developed, and in other places, a few papillae distant, there was complete absence of keratohyalin. There was decided acanthosis, with elongation of the narrow papillae. There was active migration of leukocytes in the intercellular spaces of the rete mucosa. There was some dilatation of the capillary loops in the papillae and a little round cell infiltrate about the vessels of the subpapillary layer.

DISCUSSION

DR C. W. FINNERUD. I first saw the section and considered the histologic picture a good illustration of psoriasis. Then I saw the patient and found that the section was taken from one of the psoriasiform lesions of the forearm, one of the diffuse large patches which perfectly complements the histologic picture. The section showed parakeratosis in the hyperkeratotic horny layer. There were psoriasiform proliferation and cellular infiltration. On seeing all the different types of lesions I am of the opinion that some of the histologic changes have to be accounted for by the acuity of the process and that, instead of being psoriasis, the condition is pityriasis rubra pilaris.

DR F. E. SENEAR. Not having seen the slides I did not think of psoriasis, though there were psoriasiform changes in some areas. My thought in view of the seborrheic feature on the face and with the involvement of the phalanges, despite the fact that there were no follicular plaques, was that pityriasis rubra pilaris was the most likely diagnosis. There was no involvement of the palms and soles, which may be accounted for by the acute character of the condition.

DR J. H. MITCHELL. I am inclined to agree with the diagnosis of pityriasis rubra pilaris. On the lower part of the legs there are follicular papules. The papules elsewhere are rather rounded, with some of a flat type. If the condition is not that, I do not know what it is.

DR M. OPPENHEIM (by invitation). From the clinical point of view I consider this interesting case as one of lichen planus follicularis generalisatus. I did not see the histologic slides. Some of the efflorescences, which are all located on the follicles, are polygonally shaped, have a plain surface with luster and are not prone to become confluent. The efflorescences in lichen acuminatus are much smaller, more pointed and have a spine on the top. In cases of dermatitis toxica

oozing and confluence are present. The efflorescences appear in the same order as those of lichen planus moniliformis.

DR. M. R. CARO: I think that histologically lichen planus is the one condition that can definitely be ruled out. The section I saw was compatible with the diagnosis of psoriasis. I think the follicular involvement can be accounted for in some degree by the fact that the patient has avitaminosis. I should like to see a section of tissue taken from one of the follicular papules on the abdomen.

DR. OLIVER S. ORMSBY: A few years ago I saw a patient who had symptoms resembling those seen in this patient. The condition eventually proved to be a toxic eruption. I suggest that a definite diagnosis be postponed until further observation can be made.

DR. HERBERT RATTNER: About a week ago when the man entered the hospital the picture was more that of pityriasis rubra pilaris than it is today. The lichenoid lesions are a new development.

DR. M. H. EBERT: One must bear in mind that the patient is a Negro. There is a great tendency among the Negroes to produce follicular lesions. A toxic eruption of any type may cause follicular lesions in Negroes, while it will not do so in white persons. Five or six years ago I had under observation a Negro who had what appeared to be pityriasis rubra pilaris. He was kept under observation for several weeks. The lesions faded and finally disappeared. I am convinced that he was suffering from a toxic eruption. Consequently, I am rather hesitant about making a diagnosis of pityriasis rubra pilaris in Negroes.

There seems to be some misunderstanding about the site of the biopsy specimen. It was taken from one of the early follicular lesions and not from a larger plaque. When I first saw this man the two diagnoses that suggested themselves to me were, first, acute psoriasis and, second, toxic eruption due to the medicine he had applied to the lesion. In favor of psoriasis was the presence of a palm-sized patch on the thigh with psoriatic scaling, as well as the type of scale on the follicular lesions. Kobner's phenomenon was present in at least two areas on the body, i. e., scaling follicular papules arranged along scratch marks. The appearance of the lesions has been considerably changed since that time. Ointments have been applied, which have largely removed the scaling.

The histologic findings were consistent with the diagnosis of psoriasis except for the absence of microabscesses under the stratum corneum. I think that from a consideration of the histologic picture pityriasis rubra pilaris can be ruled out. The choice lies between acute psoriasis and a toxic eruption. Psoriasis is rare in Negroes but does occasionally occur.

NOTE.—The lesions were practically clear in ten days. A diagnosis of toxic eruption appears most likely.

A Case for Diagnosis. Presented by DR. JAMES H. MITCHELL and DR. WALTER W. TOBIN (by invitation).

F. G., a man aged 54, complains of an eruption on his arms, hands and left leg of indefinite duration. He states that sores form repeatedly on his arms and hands but that they cause little pain.

The patient has been receiving antisyphilitic treatment in a city clinic since 1934 but has been irregular in attendance. Treatment was begun because of an inflammation of his right eye, which responded rapidly to antisyphilitic therapy but resulted in loss of vision of the eye. The serologic tests of the blood have given persistently positive results.

There is a masklike expression of the face, with a scar in the right cornea. The left eye is normal. The forearms, elbows and dorsa of the hands, as well as a palm-sized patch of the upper part of the left leg, show mottled erythema, whitish scars, pigmentation and ulcerated lesions. On the dorsa of the hands are several indolent bullae with serosanguinous discharge. The pain sense in the hands and forearms is greatly diminished, but the temperature sense is normal. The deep reflexes are normal.

Examination of the urine gave negative results, and the Wassermann reaction of the blood was positive

DISCUSSION

DR M H EBERT I thought the condition was factitious dermatitis. The absence of sensation was noteworthy. I inserted the point of my penknife under the skin, and the patient did not notice it. The fact that he is right handed and that most of the lesions are on the left arm is suggestive. These facts and the appearance of the lesions make a diagnosis of factitious dermatitis probable.

DR THEODORE CORNBLEET I think the changes this man shows could be accounted for by organic changes in his nervous system. I suggest syringomyelia as a possible diagnosis.

DR L M WIEDER, Milwaukee I agree with Dr Cornbleet that syringomyelia must be considered.

DR M H EBERT If I understood the history correctly, I believe the statement was made that an examination of the nervous system was made regarding the sense of heat and that of cold and that they were normal. This fact would rule out syringomyelia.

DR WALTER W TOBIN (by invitation) The masklike expression and the lowered response of the hands and forearms to pain indicates some neurologic cause. The sense of temperature is well retained. The man has had an insufficient diet, and some vitamin deficiency could well be present.

Sarcoidosis Presented by DR M H EBERT

J L, a Negro aged 47, presents multiple nodules of various sizes on the face and extremities. He first noticed small "bumps" on the face in July 1939. New lesions have appeared from time to time, and the patient states that some of the old ones seemed to disappear but not as fast as new bumps developed. He has lost about 29 pounds (13.2 Kg) in the last five years. His brother died of tuberculosis in 1910 at the age of 40.

Physical examination gave essentially negative results. The skin of the face, forehead, ears, nostrils, shoulders and forearms presents ham-colored, shiny, slightly raised, indurated papules varying in size from that of a pinhead to that of a finger nail. There are no subjective symptoms except for the papules in the nostrils, which obstruct respiration.

A Mantoux test with a dilution of 1:10,000 gave a negative result and with a dilution of 1:1,000, an area of erythema and slight edema, 1 by 0.5 cm. The Kahn reaction of the blood was negative. A roentgenogram of the hands and lungs revealed some osteoarthritis at the metacarpophalangeal articulation of the right hand and also of some of the interphalangeal joints; there was considerable rarefaction in the second phalanx of the fourth finger and possibly to some extent in the terminal phalanx; there was also a peculiar trabeculation of the second phalanx. The heart was not enlarged. There was considerable increase of the hilar markings on both sides, with slight infiltrative extension into the pulmonary parenchyma. The clinical picture is compatible with the diagnosis of sarcoid.

DISCUSSION

DR C W FINNERUD This case presents a beautiful example of superficial sarcoid of the face and other parts, cases of which in Negroes have been presented here so commonly, in most of them, however, there has been no osteoporosis or other evident signs of systemic involvement.

DR M H EBERT This is the type of condition that Dr Nomland studied and considered clinically as sarcoid. Lichenoid nodules on the alae of the nose and on the back of the neck are frequently seen in Negroes. This patient has a general adenopathy. The changes that go with sarcoid were found in the lungs on roentgen examination. There was also demonstrated a rarefaction in the

phalanges. I think this condition belongs in the same group of diseases as Besnier-Boeck-Schaumann disease.

Syphilitic Glossitis. Presented by DR. M. H. EBERT and DR. DAVID V. OMENS.

N. B., a Negress aged 25, complains of enlargement of the tongue, which was first noticed three months ago. The tongue became tender, and shortly thereafter she noticed a thick, grayish coating on the left side, extending back to the base of the tongue. With a cotton pledget she was able to remove thick thumbnail-sized pieces of brownish material from the tongue. There is no previous history of a cutaneous eruption.

The patient presents hypertrophy of the tongue. The mucous membrane is covered by a yellowish plaque, irregular in outline. On the right side, running back from the tip, there is a deep fissure extending from the tip backward, about 2 cm. long and 0.5 cm. deep. The walls of the fissure are smooth and deep. The anterior half of the left lateral wall is necrotic and covered with a yellow membrane. There is a similar fissure running from the center of the tongue to the circumvallate papillae parallel to the first. At its anterior end the fissure branches in a stellate fashion. On palpation the entire tongue is infiltrated and nodular.

The Kahn reaction was doubtful on first examination. After ten days of potassium iodide therapy the Kahn reaction was positive. The Wassermann reaction was negative on two examinations.

Histologic examination of tissue removed revealed marked perivascular infiltration, consisting principally of lymphocytes and plasma cells; there was a moderate proliferation of the endothelium.

DISCUSSION

DR. JAMES H. MITCHELL: I wonder if avitaminosis is present.

DR. H. R. FOERSTER, Milwaukee: This case is an important one for demonstration. I cannot recall when I have last seen acute syphilitic glossitis; undoubtedly the condition is uncommon and becoming increasingly so. The patients with glossitis commonly seen are in the chronic end stages with cicatricial contracture.

DR. M. OPPENHEIM (by invitation): The combination of a syphilitic condition with black, hairy tongue, as in this case, is interesting. There are two conditions of this kind: One is congenital, a nevus which does not affect the entire surface of the tongue; the other is due to irritation through certain substances.

I have succeeded in producing the condition artificially by brushing the surface of the tongue with tinctura ratanhia (Kremeriae) and other substances containing tannic acid and a red dye. I consequently came to the conclusion that all the papillae filiformes (Oppenheim, M.: *Zur Aetiologie der schwarzen Haarzunge*, *Wien. klin. Wchnschr.* 30:712, 1917). Heidingsfield stated the opinion that a certain bacterium causes this condition. Mouthwashes, tobacco and black coffee can produce in susceptible persons this condition of the tongue, which disappears spontaneously if the irritation is stopped.

DR. H. R. FOERSTER, Milwaukee: I intended to comment on the black hairy tongue. I thought the condition in this patient was not a true black, hairy tongue but a condition resulting from poor oral hygiene, possibly occasioned by the swelling of the tongue. However, considering the possibility of black hairy tongue, I think the administration of nicotinic acid is worth trying.

DR. M. H. EBERT: I appreciate the discussion on black, hairy tongue and will follow the suggestion for the administration of nicotinic acid. The reason I showed this case was well stated by Dr. Foerster. The appearance of the scarred residue of former glossitis in old cases of syphilis is familiar. So far in my experience I have never had any cases of the acute or active stage. This condition is definitely not ordinary gumma of the tongue; there is no localized sloughing. The condition of the tongue in this patient has been changed by the administration

of potassium iodide When the patient was first seen the tongue was considerably larger, and when it was grasped between the thumb and the finger there was a woody infiltrate in two areas The fissures were much deeper and open at the base With this small amount of therapy the tongue has improved greatly I believe that this case is an instance of active syphilitic glossitis

BRONX DERMATOLOGICAL SOCIETY

MARION B SULZBERGER, M D, *President*

HENRY SILVER, M D, *Secretary*

Feb 29, 1940

Sarcoidosis Presented by DR HENRY SILVER

R H, a Negress aged 25, married and childless, is presented from the clinic of Mount Sinai Hospital for Dr William Leifer She was first studied in April 1936, at which time there were lesions on the face and on the extensor aspects of the extremities A clinical diagnosis of lupus miliaris disseminatus faciei and papulonecrotic tuberculid in a patient with late asymptomatic syphilis was made Histologic examination confirmed the diagnosis of papulonecrotic tuberculid, but examination of tissue from the face revealed a picture suggestive of sarcoid Intradermal injections of tuberculin in dilutions of 1 1,000,000 and 1 100,000 gave negative reactions The blood count was normal The Wassermann reaction was positive Roentgenograms of the hands and wrists showed no changes in the bones A roentgenogram of the chest showed infiltration at the root of the right lung and enlargement of the right paratracheal glands The clinical picture suggested Hodgkin's disease

The patient was given organic and inorganic arsenic She did not continue the treatment and was not seen at the clinic until January 1938 When reexamined she stated that the cutaneous lesions had disappeared without therapy but had been reappearing gradually in the previous four months

Examination at that time showed lesions involving the auricles, the face, the lips, the trunk, the buttocks, the extremities and the fingers They were roughly of two types 1 There were numerous papules and plaquelike lesions which reached the size of a silver dollar These raised lesions were round, firm and the color of the skin or darker, some showed yellowish flecks On the face several lesions were centrally depressed and hyperpigmented 2 On the outer aspects of the arms and on the buttocks there were firm nodules in the skin or attached to it, none of the lesions were ulcerated In addition, there was generalized adenopathy, with rather disproportionate enlargement of the epitrochlear glands The spleen and liver were not palpable The tendon sheaths on the dorsa of both hands were swollen but not acutely inflamed or tender

An intradermal tuberculin test with a dilution of 1 1,000 and a patch test with tuberculin gave negative results A blood count and urinalysis showed no abnormality The Wassermann reaction was positive A roentgenogram of the chest showed distinct diminution in size of the paratracheal glands since the previous examination (April 1936) The right hilar glands were still moderately enlarged but less so than before A roentgenogram of the bones showed a cystlike area in the distal shaft of the proximal phalanx of the right middle finger Similar changes were seen in the proximal ends of the middle phalanx of the right index finger and the terminal phalanges of the three middle digits of the left hand There was a similar change in the lower end of the left ulna

Histologic examination of a plaque on the right arm showed unimportant changes in the epidermis The greater portion of the cutis was occupied by sharply

circumscribed accumulations of epithelioid cells. In the edge of one of these lobules there were a number of Langhans giant cells. A lesion on the face showed practically the same picture except that there were more giant cells. The histologic diagnosis was sarcoid of Boeck.

The patient was treated from February to May 1938 with cod liver oil, solution of potassium arsenite U. S. P. (Fowler's solution), a high carbohydrate diet and irradiation of the entire body with ultraviolet rays. The cutaneous lesions were unimproved, and there appeared swellings of the tendon sheaths on the dorsum of the right foot and above the right internal malleolus. From May 10 to August 16 she was given eleven intradermal injections of 0.1 cc. of old tuberculin in dilution of 1:100. At first there was no response to this treatment, but at the end of this period some of the cutaneous lesions had disappeared and others had flattened considerably. She was then given injections of old tuberculin in dilutions of 1:1,000 and 1:10,000.

By March 18, 1939 the cutaneous lesions were almost completely gone, but a roentgenogram of the chest showed that the process at the root of the right lung was somewhat increased and that there was enlargement of the hilar glands on both sides. There were also a faint nodular infiltration of the lower lobe of the right lung and an exaggeration of pulmonary markings on both sides. On Jan. 23, 1940 the patient stated that she felt well and had gained 10 pounds (4.5 Kg.). Most of the cutaneous lesions had disappeared, and only atrophic and pigmented spots marked their previous location. The swellings of the tendon sheath were substantially reduced. The generalized adenopathy persisted, but the individual nodes were greatly reduced in size. A roentgenogram of the chest showed enlargement of hilar glands on both sides and also of the right paratracheal glands. There was slight pulmonary infiltration. Glandular enlargement was perhaps slightly less than on the last examination. Roentgenograms of the hands showed only one cystic area, in the proximal phalanx of the right third digit.

A Case for Diagnosis (Tuberculosis of the Skin?). Presented by Dr. HARRY B. FEILER.

P. H., a Negress aged 25, was presented before this society in November 1939 (ARCH. DERMAT. & SYPH. 41:977 [May] 1940). She has since been studied by Dr. David Reisner at Sea View Hospital. A lesion of the skin, a lymph node and the tonsils were removed for histologic examination.

Microscopic examination of the tissue removed from the right elbow showed stratified squamous epithelium resting on a dense corium. Disrupting the superficial portion of the latter was a zone of extravasated blood. The corium was made up of dense fibrous tissue. It was largely replaced by discrete foci or confluent patches. These were composed of radially or concentrically arranged epithelioid cells with oval or irregular nuclei, round cells and rare giant cells. Occasionally these confluent areas disclosed an irregular central zone of pink granular material in which the outline of former cells could be discerned. The Ziehl-Neelsen stain showed no acid-fast organisms. The histologic diagnosis was epithelioid giant cell tubercles with central caseation.

Microscopic examination of an axillary lymph node showed that the normal lymphoid structure of the node was largely maintained. There were discrete or confluent foci of concentrically radially arranged epithelioid cells which contained few round cells and an occasional Langhans giant cell. There were a few areas of increased fibrous connective tissue with cells showing distorted dark nuclei. The histologic diagnosis was epithelioid giant cell tubercles and fibrosis.

On Jan. 24, 1940 a tonsillectomy was performed. The macroscopic examination showed that each tonsil was roughly ovoid and measured approximately 2 by 1 by 1 cm. The pharyngeal surface was smooth and cryptic. On section each tonsil exhibited a 1 to 2 mm. round yellow-white focus, with a poorly defined capsule.

The microscopic examination showed that the tonsils were largely replaced by discrete or confluent cellular foci of radially and concentrically arranged epi-

thelioid cells with small irregular or large oval vesicular walls. There was a moderate number of round cells in the foci. Giant cells were rarely noted. The histologic diagnosis was epithelioid cell tubercles.

DISCUSSION

DR DAVID REISNER (by invitation) I am glad to have the opportunity of discussing the question of sarcoid before a group of dermatologists, since they are chiefly responsible for valuable investigations of the cutaneous as well as the systemic manifestations of the disease. Its systemic character is of particular interest to me as an internist.

I have studied the case presented by Dr Feiler. It is a good example of the association of cutaneous lesions and involvement of the lymphatic system, including the tonsils. My observations indicate that systemic involvement of the lymph nodes is probably the most constant finding in sarcoidosis and that great enlargement of the mediastinal and hilar nodes is one of its outstanding features. However, these changes are only a part of a widespread generalized process which involves various organs or anatomic systems such as the lungs, skin and bones and more rarely the eyes, spleen, liver, parotid and other salivary glands, mucous membranes and lacrimal glands.

I wish to emphasize a few principal points. First, the disease referred to as "sarcoidosis" is inherently a generalized process with a predilection for certain organs or structures. Secondly, while cutaneous manifestations are often present, they do not constitute an essential part of this entity. Thirdly, localization in various organs and their combinations produces a variety of clinical syndromes which have been described under various designations, such as uveoparotitis (in some cases presenting features of Mikulicz' syndrome), atypical tuberculous splenomegaly, Jungling's disease of the bones and large cell hyperplastic tuberculosis. These various types represent only clinical variants of an identical basic pattern.

DR SAMUEL M. PECK The internists should not lose sight of the fact that for more than fifteen years dermatologists have stressed osseous, pulmonary and other involvements as part of the picture of generalized sarcoidosis. The fact that tuberculin anergy is discussed in connection with this disease shows that the dermatologists have taken into account systemic relations. With respect to the histologic picture, a diagnosis is easily made when typical epithelioid cell tubercles are present. Unfortunately, this classic picture is often wanting, and the histologic findings must therefore be evaluated only in association with the clinical picture. It is admitted by all who have experience with the tuberculin test in cases of sarcoid, both the localized and the generalized form, that the test tends to give negative results. Even in the same patient the degree of sensitivity may vary from time to time. This holds true especially for tests for immune and allergic states.

DR DAVID BLOOM Judging from the literature, the eruptions recorded as belonging to the group of sarcoidosis rarely show the characteristic histologic picture of sarcoid. I believe that these eruptions fit best into the group of disseminated tuberculosis, seen mostly in the Negro. There must be a special immunity factor in the Negro responsible for this type of attenuated tuberculosis.

DR GIRSCH D. ASTRACHAN I am interested in the question of therapy, and I was much impressed with the results obtained in these cases. About a year ago I presented before this society a case of sarcoid of Boeck and Darier-Roussy sarcoid (*ARCH. DERMAT. & SYPH.* 40:850 [Nov.] 1939) which was complicated by tumor formation of the superior mediastinum and leukopenia. All kinds of medications, including liver extract, high vitamin diet, iron and filtered roentgen rays were without benefit. Can Dr. Reisner suggest other methods of therapy?

DR DAVID L. SATENSTEIN I was taught long ago that it is not safe to take anything for granted. What factors are necessary for a diagnosis of tuberculosis? The fact that the tissue suggests it is in itself not sufficient. A positive reaction

to tuberculin, positive results of animal inoculations and the presence of tubercle bacilli are the necessary criteria.

Sarcoidosis is a condition in which the tissue suggests some form of tuberculosis, as is so frequently reported. However, organisms have not been demonstrated, the patient did not react to tuberculin, and animal inoculations were not conclusive; yet the condition is labeled "some form of tuberculosis."

I have had little experience in treating patients with generalized sarcoidosis, but I have seen and studied many local sarcoids. Clinical lupus vulgaris presents occasionally the microscopic picture of sarcoid; conversely, clinical sarcoids may present the microscopic picture of a low grade lupus vulgaris. At other times both lupus vulgaris and sarcoids may present the microscopic picture of granuloma annulare.

If one asserts that because sarcoid lesions are present in a suspected tuberculous person the sarcoid is some form of tuberculosis, then by the same reasoning lupus erythematosus must also be regarded as some form of tuberculosis since that dermatosis also occurs in combination with sarcoid. Such an assumption is unwarranted. At the present time and until more is learned about the process, the law must be laid down that a diagnosis of tuberculosis needs to be proved, i. e., as to tissue reaction, organisms, reaction to tuberculin and positive animal inoculation.

I am not prepared to accept sarcoid as some form of tuberculosis on the tissue findings alone, as this type of tissue change is noted in a number of other dermatoses which have nothing in common with or no relation to tuberculosis.

DR. MARION B. SULZBERGER: I agree with the majority of the remarks of the previous speakers with the exception of certain opinions expressed by Dr. Satenstein which are at variance with those of most investigators who have studied this disease. An important point is that in most cases of this condition in Negroes the picture is certainly not representative of typical sarcoid. Negroes suffering from sarcoids often have in addition some other forms of cutaneous tuberculosis; one rarely finds a pure sarcoid in the Negro. On the other hand, in the white race it is rare to find sarcoid lesions associated with other forms of cutaneous tuberculosis.

I had the opportunity of seeing 3 of Dr. Reisner's patients. Two of them had lesions that did not impress me as sarcoids. The third had lesions both of sarcoid and of lupus vulgaris. The young Negress presented this evening impressed me as having lupus miliaris disseminatus rather than sarcoid, particularly as regards the lesions on the nose and eyelids. In discussing the problem of sarcoid, it is important to distinguish these forms. Lupus miliaris disseminatus faciei, lupus vulgaris and sarcoid show a different histologic picture, course and response to tuberculin and differ in other respects.

Furthermore, the fact that sarcoid is a systemic disease has long since been recognized by dermatologists. On the whole, this subject is certainly less new to the dermatologist than to the internist. I must emphasize that when one finds caseation in a lesion one is no longer justified in calling that lesion sarcoid. Caseation is typical of lupus miliaris disseminatus faciei, and necrosis is often present in other tuberculoderms, such as scrofuloderma and lupus vulgaris. In the latter, the reaction to tuberculin is likely to be positive and bacilli will be found. One has to be critical, and one certainly cannot say that Dr. Reisner's observations in the Negro are typical of sarcoidosis or sarcoid, for the Negro generally presents mixed and transitional forms rather than pure sarcoidosis of the type usually seen in the white race.

DR. LOUIS CHARGIN: There appears to be an interplay between sarcoidosis and tuberculosis. So far no definite proof exists, histologic, clinical or biologic, that the two diseases have a common causation. Lomholt (*Acta dermat.-venereol.* 18:131-149, 1937) reported that in cases of sarcoid the tuberculin reaction was positive in 25 per cent, negative in 25 per cent and doubtful in 50 per cent.

DR. DAVID REISNER (by invitation): The relation between sarcoid and tuberculosis is of interest. I am well aware of the long-standing controversy on this

particular point It cannot be denied that this question has not been answered to complete satisfaction as yet I should like to mention only briefly some of my own observations which may have a bearing on this issue Tissue from one of my patients with sarcoid gave a positive result on guinea pig inoculation In some cases after a long period of observation active and progressive pulmonary tuberculosis developed In other instances cutaneous lesions, which both clinically and histologically appeared to be lupus vulgaris, coexisted with widespread lesions characteristic of sarcoid This is not mere coincidence I may also add that the presence of necrosis does not necessarily militate against the diagnosis of so-called sarcoidosis, for varying degrees of caseating necrosis have been found in a number of biopsy specimens which in all other respects presented classic features of systemic sarcoid It may perhaps be argued that I have been inclined too frequently to the diagnosis of sarcoidosis It seems to me, however, that the borderline cases are of great significance from the pathogenetic point of view I have used the term "so-called sarcoidosis" advisedly, as it is often extremely difficult to draw a sharp line between sarcoid and tuberculosis, that is, to state definitely where and when the former stops and the latter begins

Both the clinical experiences and the histologic findings seem to suggest that what is called sarcoid does not represent a static entity but a certain peculiar form, or phase, of an attenuated systemic tuberculous infection, which under certain circumstances may be directly transformed into progressive and destructive tuberculosis Why this extraordinary behavior exists and whether it is due to an alteration or variability in the virulence of the infectious agent or the result of an unexplained immunobiologic state of the host are of course questions of principal importance to which no adequate answer can be offered on the basis of present knowledge

DR SAMUEL M PECK The tuberculin test in cases of sarcoid is used for the purpose of diagnosis and not as a support for the theory of tuberculous causation Furthermore, it is of diagnostic significance only if the result is negative There are, however, a number of facts which must be explained in connection with the negative reaction to tuberculin in cases of sarcoidosis before a tuberculous causation is denied Those patients who have a negative reaction to tuberculin show the presence of anticutins If these immune bodies are not a proof of causation or relation that is specific, they must be relegated to the class of Forssman antibodies Such a conception in itself is of extreme interest

DR MAURICE UMANSKY The conception of specific anergy cannot be explained solely on the basis of the presence of percutins The percutins were searched for and not found in some cases of sarcoidosis in which there were negative reactions to tuberculin The tuberculous nature of the condition in the cases presented tonight seems to be well founded Other types of sarcoid reaction of the tissues are less likely to be due to the tubercle bacillus Opinions were expressed that sarcoidosis is a condition *suu generis* produced by an independent micro-organism It is possible that the causative agent suppresses the allergic response to tuberculin the same way as it does in measles or scarlet fever, causing temporary anergy

DR MARION B SULZBERGER One cannot form an opinion on this subject without studying many cases and performing many animal inoculations and serologic studies Moreover, one must be well acquainted with the many careful studies of other investigators No mention has been made, for instance, of animal experiments It is a difficult subject, and there is room for argument However, the bulk of the evidence is pretty strongly in favor of the tuberculous nature of many examples of sarcoid Note that I say not all but many, for it is known that sarcoid can be produced by leprosy and syphilis However, in most of the cases there is evidence that the tubercle bacillus plays a role in this type of lesion What additional proof would one desire than these Negro patients of Dr Reisner? For in Negroes one often sees lesions due to tubercle bacilli, such as scrofuloderma, lupus vulgaris and papulonecrotic tuberculid, combined with typical sarcoid of the skin and internal organs This demonstrates that sarcoid lesions and lesions of true tuberculosis are associated in the most intimate possible manner

DR. WILLIAM LEIFER (by invitation): During the long period of observation of our case the eruption cleared spontaneously on one occasion. When recurrence took place the patient was given injections of tuberculin followed by a complete disappearance of the cutaneous lesions. It is apparently difficult to evaluate therapeutic measures in this disease.

DR. HENRY SILVER: The concept that sarcoid is an outward manifestation of a more widespread systemic disease is gaining ground. This evening's discussion has brought out clearly the internist's and the dermatologist's point of view. It is of interest that there is so much agreement in principle.

In cases of systemic sarcoidosis the involvement of the organs in the order of their frequency is: lymph nodes, lungs, skin, bones and other organs, such as the spleen and liver. In Dr. Reisner's series cutaneous lesions were present only in 8 cases of 23. The cutaneous lesions vary in shape and size, but they all have fairly typical sarcoid structure histologically. To the internist the various dermatologic types of the disease are irrelevant. To him the disease entity is important. There can be no quarrel with such a conception. It is evident that too much stress should not be laid on clinical appearance in sarcoidosis. In my case, for instance, the clinical aspect suggested first lupus miliaris disseminatus faciei, and only after these lesions disappeared were typical sarcoid lesions seen. The spontaneous retrogression of cutaneous lesions and systemic manifestations in sarcoid cannot be too strongly emphasized, as is well shown in Reisner's cases. This is important in the interpretation of our therapeutic measures and in the prognosis of the disease. I am referring particularly to the frequent argument of the relative value of various forms of therapy (Chargin, L.: *ARCH. DERMAT. & Syph.* 36:458 [Aug.] 1937; 40:493 [Sept.] 1939).

The controversial discussion of the tuberculous causation of sarcoid will probably continue in spite of the many clarifying points brought out tonight. In favor of the tuberculous causation are: (1) Kyrle's case in which tubercle bacilli were demonstrated in the earliest stages of the disease (Kyrle, J.: *Arch. f. Dermat. u. Syph.* 119:117, 1914); (2) the histologic picture, which simulates the productive form of tissue reaction often seen in lesions of unquestionable tuberculous origin; (3) the fact that patients with sarcoidosis show coexisting caseating tuberculosis, and (4) postmortem findings of classic tuberculous changes in 50 per cent of cases. I agree that more studies in this direction are necessary to prove definitely the tuberculous causation.

Erythroderma Ichthyosiforme Congenitale. Presented by DR. ADOLPH ROSTENBERG.

The patient, a woman aged 19, was born in the United States. There is no consanguinity. The patient had diphtheria during childhood but no other ailments. According to the mother's statement the cutaneous condition began at the age of 2 years. She has never been free of the disease. During the summer months the skin appears to be paler. At times there is slight itching.

The most pronounced feature of the cutaneous condition is the generalized erythroderma. The face appears red and glossy, the redness being most evident about the nose. There is profuse scaliness of the scalp. On the neck, chest, back and abdomen the erythema is almost diffuse except for a few small normal areas, which give the impression of a bizarre and gyrate picture. The skin in these areas is infiltrated, and there is continuous branny desquamation. The extensor surfaces of the upper extremities are greatly involved, whereas the flexor surfaces are comparatively free of eruption. The skin on the dorsal surfaces of the hands is thickened, and over the second phalanges of several fingers follicular plugs are noticeable. The palms and soles are not involved. The skin of the buttocks and the lower extremities, especially on the flexor surfaces, is considerably thickened, showing the characteristic picture of mild ichthyosis.

Physical examination gave negative results. Urinalysis showed no abnormalities. The Wassermann and Kahn reactions were negative. The blood count, including the differential count, was essentially normal.

DISCUSSION

DR DAVID BLOOM The fact that the extensor surfaces of the extremities are involved and the flexor surfaces free would be against a diagnosis of erythroderma ichthyosiforme congenitale as described by Brocq

DR DAVID L SATENSTEIN I am willing to accept Dr Rostenberg's concept of these cases. The functional derangement or anomaly was probably present before birth or at birth, but the patient did not show clinical manifestations until the age of 2 years. There are other conditions that do not manifest themselves until puberty or even later in life which are still regarded as congenital anomalies.

DR HENRY SILVER I have studied the case with Dr Rostenberg at the Bronx Hospital. I must admit that in spite of repeated observations of the case I am still undecided as to the diagnosis.

The diagnosis of erythroderma ichthyosiforme congenitale was suggested at the outset. Certain features, however, are lacking, such as consanguinity, involvement of cubital and popliteal regions, keratosis of the palms and soles, increased hair and nail growth and disturbances of other ectodermal tissues. In Jadassohn's handbook (Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1931, vol. 8, pt. 2, pp. 18-19) 2 cases are recorded in which there was a similar picture, 1 by Nicholas and Jambon and the other by Mendes da Costa. In both cases the condition is regarded as a variety of erythroderma ichthyosiforme congenitale and is described as erythroderma and keratoderma variabile or keratosis rubra figurata (Rille). These conditions are transitional forms which bridge congenital ichthyosiform erythroderma and congenital keratoderma. The variability of the clinical picture is one of the main difficulties in arriving at a correct diagnosis.

DR ADOLPH ROSTENBERG Considering the fact that the disease, according to the patient's mother, appeared when the patient was 2 years old, it is probable that the condition was already present at birth. This would not speak against its congenital nature. In most of the reported cases the disease was noticed at the age of 2 years or even later.

There are features in this case which differ from those in the majority of the reported cases, i. e., the mildness of the ichthyosis and the involvement of the extensor surfaces of the upper extremities rather than the flexor surfaces. The case can hardly be classified as one of ichthyosis because of the existing erythroderma.

A Case for Diagnosis (Fungating Iodide Eruption of the Tongue? Squamous Cell Epithelioma of the Tongue?) Presented by DR MARION B SULZBERGER

S. M. a man aged 62, was first seen with Dr Milton Rosenbluth and Dr J. William Hinton on Feb. 18, 1940. He had suffered from thyrotoxicosis for many years. He had had a partial thyroidectomy twenty years before. The first week in February 1940 he had again been operated on by Dr Hinton (thyroidectomy). Preceding the operation he had received iodides by mouth for some time, but the administration had been discontinued afterward.

The lesions of the tongue had first been observed about the middle of January. The condition was said to have commenced as a raw, beefy and somewhat swollen tongue, and as the rawness and swelling subsided, two isolated, discrete tumors became visible, one on the dorsum of the tongue near the left side of the tip and the other on the dorsum about $1\frac{1}{2}$ inches (0.7 cm.) farther back and on the left side of the median line. These tumors grew rapidly, so that they began to interfere with the patient's eating.

At the time of the first examination the tumor near the tip of the tongue was small, roughly hemispherical and the size of a pea, the other was lozenge shaped and the size of a bean. Both tumors were elevated, rising about $\frac{1}{4}$ inch (0.1 cm.) above the surface. They were separated by intervening approximately normal tongue tissue, the surface, however, was flattened and devoid of papillae. Immediately surrounding the larger tumor the papillae were not only preserved but

slightly elevated and perhaps slightly hyperkeratotic. The tumors were freely movable and not visibly ulcerated. They were flat topped, with a whitish coated surface, and were mushroom-like, each having a slightly narrowed, somewhat stalklike peduncle. The area of the tongue surrounding the base was not infiltrated or reddened. The remaining skin and mucous membranes were apparently normal. There were no palpable lymph nodes.

On February 19, with local anesthesia, both tumors were clipped off at the base of the stalk, and the clean-looking, slightly bleeding surface was lightly sparked by electrodesiccation. Healing was uneventful.

The tissue of both tumors was divided into two parts and sent to two pathologic laboratories. Slides of the sections prepared by Drs. Satenstein and Sachs were, with their consent, sent to two other pathologists of large experience. All those who studied the slides were furnished with a detailed description of the clinical appearance and history of the case.

Dr. David L. Satenstein and Dr. Wilbert Sachs reported as follows: "Both sections showed the same type of process. Extending down to the bottom of the section from the lower border of an irregularly acanthotic epidermis was a large epithelial mass arranged in strands and bands and isolated cells. About this were numerous small dilated vessels and a substantial cellular infiltrate which was composed chiefly of polymorphonuclear leukocytes and some small round cells. The palisade layer was entirely missing. The cells composing the mass were of different sizes, most of which were large. They had large, oval, fairly well stained nuclei; the cytoplasm was faintly stained, and the cell outlines were visible. Some of the cells were multinucleated. There were numerous mitotic figures present but no pearls or whorls. The histologic diagnosis was infiltrating undifferentiated epithelioma."

Dr. Henry R. Muller reported as follows: "Microscopic examination showed two pieces of firm grayish white tissue. The larger piece of tissue measured approximately 1 cm. in length and 0.5 cm. in width, whereas the small piece measured 0.5 cm. in length and less than that in width. Both were embedded in 'toto' for sectioning. Microscopic examination of the larger piece showed a benign papilloma derived from squamous epithelium. Associated with it was an area of purulent inflammation in granulation tissue. In this area there was considerable proliferation of endothelial cells. Mitotic figures were present. The surface was necrotic, and bacterial colonies were seen in it. The small piece of tissue consisted almost entirely of granulation inflammatory tissue, with much necrosis and bacterial growth in the surface layers. A small piece of normal squamous epithelium was attached. The histologic diagnosis was papilloma (in one piece) and granulation tissue, with purulent exudate, necrosis and bacterial growth (both pieces)."

Dr. James Ewing reported as follows: "The sections of lesions from the tongue were difficult to interpret. There were features which strongly suggested a diffuse epidermoid carcinoma, and I do not wonder that this diagnosis has been made. However, the structure lacked the definite features of infiltrating squamous carcinoma. The large cells were probably vascular endothelium. The whole lesion was richly infiltrated with polymorphonuclear leukocytes. Mitotic figures were remarkably abundant. There were a great many new blood vessels. There was superficial ulceration. The history of long administration of iodine raised the question of iododerma. Comparing this section with those of other cases of iododerma in my collection, I find the structure exactly duplicated. I think therefore that the condition is not a malignant process but a remarkable form of iododerma. The case is of so much interest that I should appreciate being allowed to keep the sections to add to my collection."

Dr. Paul Klemperer reported as follows: "Section showed a fragment of tongue somewhat mushroom-like in shape. The stalk of the mushroom was lined on either side by regular squamous epithelium, while the upper part was extensively ulcerated on the surface. The stalk consisted mainly of muscle; the lower part of the cap adjacent to the stalk showed heavily inflamed stroma, while the upper portion of the cap consisted of large polygonal cells with abundant cytoplasm

and large round or oval nuclei, with a fine chromatin network and one or two nucleoli. These cells showed frequent atypical mitoses. Only at the periphery adjacent to the surface epithelium did the cells form islands, elsewhere they were generally separated by polymorphonuclear leukocytes. The histologic diagnosis was immature squamous cell carcinoma with ulceration."

After he saw Dr Ewing's report, Dr Klemperer made the following additional report: "I am much impressed by Dr Ewing's diagnosis. I have compared the slides with those of Eller's case, which I had occasion to study some years ago, and there is certainly a good deal of similarity between them. Apparently I missed the point that the patient had received intense iodide therapy. I recall only that he was operated on for toxic goiter. Of course, I have compared the cells in question with the squamous epithelial cells of the adjacent skin and found also great similarity. For this reason, I have made the diagnosis of squamous cell carcinoma. It seems to me that the final diagnosis will depend on the further clinical events in the case, but I do believe that the resemblance to Eller's case is striking."

DISCUSSION

DR DAVID L. SATENSTEIN: In the past I have had the opportunity to study the various stages of cutaneous reaction to iodides. In the early stage there is a perivascular lymphocytic infiltration similar to that seen in the early stage of lymphatic leukemia. Later there are two types of processes. One (the more common) develops into the clinical vesicopustular stage, in which there is a liquefaction of the cutis, with secondary changes in the epidermis, and the other, which is rare, is the clinical tuberosus form. In this type there is a tissue reaction which is difficult to differentiate from mycosis fungoides. Whatever the changes that take place in an iodide eruption, the changes of the epidermis are always secondary to those of the underlying cutis. In Dr Sulzberger's case there were projections of undifferentiated epithelial cells extending downward from the under surface of the epidermis. The cutis reaction about these zones was similar to that seen in early infiltrating epithelioma of the anaplastic type.

I doubt the accuracy of the history and observation as to the duration of the lesions. They were probably present for some time, and the accompanying inflammatory reaction seems to have accentuated the development of the lesions. The tentative diagnosis of anaplastic epithelioma is preferable to that of an iodide eruption.

PHILADELPHIA DERMATOLOGICAL SOCIETY

J. V. KLAUDER, M.D., *Chairman*

HERMAN BLERMAN, M.D., *Secretary*

March 15, 1940

Symposium on Cutaneous Diseases in Animals

Introduction Presented by DR J. V. KLAUDER

Symposiums on cutaneous diseases in animals have occasionally been held at meetings of dermatologic societies in Europe but, to my knowledge, never at such meetings in this country, certainly this is the first one in the history of the Philadelphia Dermatological Society. For this privilege the society is indebted to Drs William L. Lentz, Mack A. Emmerson and Harry M. Martin, of the faculty of the School of Veterinary Medicine of the University of Pennsylvania.

There should be a close relation between veterinarian schools and medical schools in the study and teaching of diseases that occur both in man and in animals. I hope that the time is not too far distant when a chair of comparative

medicine will be created in medical schools. As a matter of fact, Dr. Herbert Fox is professor of comparative pathology in both the medical and the veterinary school at the University of Pennsylvania.

The exhibit on cutaneous diseases in animals at the Ninth International Congress of Dermatology in Budapest, the representation of comparative dermatology on the program of this congress, Henry and Bory's chapter, "Studies of Comparative Dermatology," in "Nouvelle pratique dermatologique" (Henry, A., and Bory, L., in Darier, J., and others: *Nouvelle pratique dermatologique*, Paris, Masson & Cie, 1936, vol. 3, pp. 753-894), a similar chapter by Heller in *Jadassohn's handbook of Krankheiten*, Berlin, Julius Springer, 1930, vol. 14, pt. 1) and the illustrations of (Heller, J.: *Tierdermatosen*, in *Jadassohn's handbook of Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1930, vol. 14, pt. 1) and the illustrations of cutaneous diseases in animals in "Corpus iconum morborum cutaneorum (Nékám, L.: *Corpus iconum morborum cutaneorum*, in *Deliberationes Congressus dermatologorum internationalis*. IX, Budapestini, Sept. 13-21, 1935, Leipzig, Johann Ambrosius Barth, 1938, vol. 5, pt. 3, pp. 848-867) are evidence of the importance and the increasing interest in comparative dermatology.

The dermatologist can profit from a knowledge of cutaneous diseases in animals. For example, a morphologic visualization of cutaneous lesions should include the unique and curiously shaped, round, rectangular, quadrangular and rhomboidal lesions occurring in swine erysipelas. The longer the duration of the infection in man (erysipeloid of Rosenbach), the greater is the tendency for the morphologic appearance of the lesions to resemble that of the lesions in swine. Knowledge of a disease is naturally more complete if it can be studied in animals. I do not refer to the infectious diseases that have been experimentally produced in animals, the history of which furnishes an important illustration of the evolution of the modern knowledge of medicine. I refer to the diseases of man that occur naturally in animals, for example, sarcoma, eczema, pruritus, alopecia areata and seborrheic dermatitis. It appears to me that etiologic and other considerations of such diseases are not complete unless the disease is visualized in animals. In pruritus in dogs, for example, there appears to be a psychogenic aspect, and in eczema in animals, diet apparently plays an important role. Moreover, a dog with eczema is an admirable laboratory specimen for the study of this disease. A discussion of lymphoblastoma is not complete without including the so-called syphiloid of cats. Bory stated the belief that this lesion is the analogue of the Paltauf-Sternberg form of lymphogranuloma in man.

Investigation conducted in the domain of veterinary medicine may profitably engage the attention of the dermatologist. Studies of the sulfur content of wool and its relation to the sulfur content of the soil and of the fodder of sheep have been contributions to the knowledge of the role that metabolism of sulfur plays in the development and growth of keratin. Photosensitizing of animals is likewise of interest to the dermatologist. In white or white-spotted swine or cattle fed on buckwheat and exposed to the sun dermatitis (sparing pigmented areas) and constitutional symptoms (buckwheat poisoning, or fagopyrism) develop. Buckwheat contains phytoporphyrin, a derivative of chlorophyll, which closely resembles chemically porphyrin and mesoporphyrin.

Pathologic states in animals and their investigations by veterinarians have a direct relation to human medicine. One illustration of this relation is the disease known as parturient paresis or milk fever of cows, which also occurs in sheep ("lambling sickness"). In this disease there is a considerable decrease in the calcium and phosphorus content of the blood. Symptoms of tetany which characterize the disease are thus explained. These symptoms are dramatically relieved by an intravenous injection of calcium.

The dermatologist may profit from the observations of veterinarians. Dr. Lentz recently told me of a dog in his care which after the birth of her litter did not eat the placenta and suffered an extensive loss of hair. In studies conducted by Brown and me, alopecia in women after pregnancy apparently could not be attributed to a disturbance of sulfur metabolism. An endocrine basis appears to be a reason-

able assumption. These circumstances suggested to me the use of placenta extract in treatment of loss of hair in women after pregnancy. After using this therapy, however, I could not conclude that it was of value.

Presentation of Cases and Lantern Slides Presented by DR WILLIAM J LENTZ (by invitation), Professor of Veterinary Anatomy, School of Veterinary Medicine, University of Pennsylvania

Ichthyoid Skin in a Bull Dog—This condition has been present throughout the entire life of the animal. I have never seen ichthyosis in dogs heretofore.

Microsporon Infection in a Dachshund—The kind of microsporon is unknown.

Staphylococcic Dermatitis in an Irish Setter—This dog had a neurogenous background. It was hospitalized one week in a quiet place, with treatment. The lesions improved greatly. There has been no change in the dog's diet since its admission to the veterinary hospital.

Alopecia in an Irish Setter—A diet too rich in carbohydrates caused the condition. Correction of the diet was followed by recovery. Overfeeding is a most important factor in eczema of dogs. The condition may also result from an absence of fat in the diet.

Patchy Eczema in Dogs—These two dogs were extremely nervous and scratched themselves at the sight of another dog. There was improvement by feeding them every other day instead of once daily. The diet consisted at first simply of milk and commercial dog food.

Follicular "Mange" in Dogs—This condition was found in a cocker spaniel and a bull terrier. There are two types of follicular (or demodectic) mange, squamous and pustular. I believe that dogs with ichthyoid skins are predisposed to the squamous type of mange. The disease is not contagious, dogs can be put in a kennel with others with little likelihood of their being infested. From a single hair follicle of an animal with the pustular type one can squeeze hundreds of organisms. Treatment consists in keeping the dogs clipped and giving them fresh air, sunlight and a strictly carnivorous diet containing some fat. In some cases the condition appears to be self limiting. The pustular type is often associated with renal disturbance and emaciation.

Dermoid Tumor of the Eye—This condition occurred at the outer canthus of the eye of a dachshund. It was treated by dissection.

Ringworm in a Fox Terrier—The infection was contracted from a stray cat. A man, his wife and their child also contracted the disease.

Multiple Furunculosis in a Scotty—This dog has been fed largely on vegetables, bread and dog biscuit. Dogs fed on vegetables are predisposed to pruritus. The absence of cellulose-splitting organisms in the dogs' intestines may be a factor in this predisposition. This dog also has nephritis.

Generalized Eczema in an English Bull Terrier—This dog had the worst eczema I have ever seen, but the condition responded almost immediately to autohemc injections and to dietary correction.

DISCUSSION

DR WILLIAM J LENTZ (by invitation) Dogs with follicular mange have surprisingly little pruritus. That is, of course, diametrically opposed to scabies (caused by *Sarcoptes scabiei*).

DR A STRAUSS Does the cat tolerate arsenic better than the dog?

DR WILLIAM J LENTZ (by invitation) I think the dog tolerates arsenic better than any other animal. It is surprising what large doses the animal will tolerate. In New Orleans, where the incidence of filariasis (heart worm disease) is so high, a veterinarian told me that he had given as high as 20 to 25 grains (12 to 15 Gm) of arsenic in one dose. He said that this dose either kills or cures. I have given a total dose of 20 grains (12 Gm) of arsenic to a dog, without deleterious effect, so far as I could ascertain. I have also frequently

given 1 grain (0.06 Gm.) of arsenic daily for long time safely and with improvement in the animal's condition. Recently I saw a pointer which was so emaciated that the owner wished to have it destroyed. I used this dog to test the extent to which he would tolerate fat. He was fed suet and $1\frac{1}{2}$ pints (710 cc.) of milk daily and became fat. I have no explanation for this observation. I have observed many cases of eczema in the dog due to the omission of fat from the diet. For some reason or other, the public believes that dogs should not have fat, but I believe the treatment for some cases of eczema is simply to give fat. Part of the reluctance to give fat arises from the fact that it becomes rancid. Its omission from dogs' diets may explain why in some kennels many dogs are found with coat, skin and body in poor condition.

Roentgen Rays in the Treatment of Diseases in Animals. Presented by DR. MACK A. EMMERSON (by invitation), Assistant Professor of Veterinary Surgery and Obstetrics.

Roentgen ray therapy in the treatment of the diseases of animals is new, especially in this country. Nevertheless, many experiments have been carried out on the dog. What I have to offer this evening are the results obtained in the various species of animals. The skin of a Jersey cow was found to tolerate at least twice as much roentgen radiation as that of a man, when given at a single dose.

I have never seen in a large animal, that is, a horse or a cow, any sign of a cutaneous erythema as the result of irradiation. One of the first effects to be noted is discoloration of the hair, and then, if the dose is large enough, epilation and vesiculation occur. As a result of various tests on the cow, I found that this animal's epilation dose is 1,250 r. Professor Pommer, of Vienna, has ascertained that the epilation dose on the heavily haired parts of the body of the dog is between 1,080 and 1,200 r. I have experimented and found that in the sparsely haired parts of the dog's body I can produce erythema and temporary epilation with between 650 and 750 r. On the more heavily haired section of the body between 1,080 and 1,200 r is required to produce epilation, with no signs, again, of erythema.

Actinomycosis of the Mandible of the Cow.—The cow was given 2,026 r in five treatments, with decided improvement in the physical condition of the animal but poor results from the standpoint of destruction of the fungus.

Carcinoma of the Third Eyelid Extending onto the Orbit in a Western Horse.—This condition was treated with 2,000 r, and the result has been good.

Hoof Canker in a Horse.—The condition in this case responded favorably to 1,600 r to each foot, in four treatments over two weeks, but it later recurred. The experience of the Viennese, however, in similar cases has been disappointing.

Scotty with an Interdigital Cyst (Epidermoid Carcinoma).—This lesion was removed surgically on July 26, 1938. By July 29 the growth had recurred and was larger than the original cyst. It was found histologically to be an epidermoid carcinoma. Involution was brought about by 812 r of roentgen rays in two treatments. The animal lived about a year and then died of a severe hemorrhagic gastroenteritis and extreme renal fibrosis, but with no recurrence or metastasis.

Collic with Inoperable Epidermoid Carcinoma of the Paw.—In this dog, which was 15 years old, 2,500 r caused a partial clearing up in two weeks of the visible process. The dog has survived for eighteen months without evidence of metastasis, although the original involvement is not entirely gone.

Wire-Haired Fox Terrier with Anal Carcinoma.—This 4 year old female dog was treated with roentgen rays from September to October 1938, for anal carcinoma. In the eighteen months since then there has been no recurrence.

Dachshund with Carcinoma at the Site of Removal of an Incisor Tooth.—The lesion was treated with roentgen rays twice, with a total of 900 r. The dog died in November 1939 of severe gastroenteritis, but no metastases were found at autopsy.

Dog with Sarcoma on the Inside of the Cheek—The dog, a cross between a shepherd and a collie, a 12 year old male, was given 2,800 r, in four treatments in eight days, followed by surgical removal of the tumor. An additional 1,200 r in two treatments was administered after the operation. The local lesion regressed completely under this treatment, but at the postmortem examination six months later, lesions suggestive of metastasis were found in the lungs.

Sarcoma in the Axillary Region of a Beagle—This animal was given two series of treatments, totaling 8,000 r. It died six months later of generalized lymphosarcomatosis with jaundice, the result of occlusion of the bile duct by the tumor.

Digitate Verruca on the Inside of the Ear of a Dog—This lesion completely regressed after treatment with 1,500 r in four weeks.

Sublingual Papilloma (Carcinoma?) Involving the Side of the Cheek of a Dog—This dog received nine treatments of 1,600 r over fifty-three days, with complete regression of the lesions. They subsequently recurred and are now responding to a second series of roentgen ray treatments.

Multiple Verrucae in the Mouth and on the Gums of a Dog—These lesions, which had previously resisted all forms of treatment, were given two treatments totaling 600 r and showed great improvement at the second treatment. The animal was supposed to return for a third one, but he never came, and, according to verbal report from the owner, the lesions disappeared completely.

Nonspecific Granuloma on the Dorsum of the Tongue of a Dog—After three roentgen ray treatments, the large lesion was removed surgically, and there has been no recurrence.

Cancer of the Anus in a Harlequin Great Dane—This 3 year old animal has received 2,000 r in six treatments spread over fifteen days and now has only a small, nonpigmented papule at the anus.

Epidermoid Carcinoma of the Vulva in a Shetland Pony—The animal received 2,500 r in five treatments over nine days, and the lesion rapidly improved. There has been no recurrence to date.

DISCUSSION

DR A STRAUSS Do carcinomas metastasize in animals as they do in human beings?

DR MACK A EMMERSON (by invitation) From my limited experience, I should say that they do.

DR JOHN B LUDY Has a special examination of the skin of the dog shown a greater content of metal than in the skin of a human being? If it did, would that account for the fact that larger doses of roentgen rays can be given?

DR MACK A EMMERSON (by invitation) I cannot answer that question.

DR FRED D WEIDMAN Of course the feathers of birds contain quantities of copper, do they not?

DR MACK A EMMERSON (by invitation) Yes.

DR FRED D WEIDMAN Is there any in the skin?

DR MACK A EMMERSON (by invitation) I do not know. I thought the pigment in the hair and skin was possibly responsible for the large doses of roentgen rays which animals can stand, because in the nonhairy areas they cannot stand nearly so much. They can stand it on those hairy areas even with the hair clipped off.

DR WILLIAM J LENTZ (by invitation) It would appear that the skin of the dog has great powers of absorption, perhaps greater than the skin of man. Some years ago Dr John Marshall shaved the side of a dog's chest and then painted it with a commercial hair dye containing lead and in forty-eight hours recovered lead from the spleen and liver. In my experience I find that dogs do not stand mercury well. Of course with pediculosis many persons use ammoniated mercury and set up a mercurialism in a short time. Dogs seem to absorb about

everything applied to the skin. That is why one has to be so careful in applying medicaments to their skin.

DR. THOMAS BUTTERWORTH, Reading, Pa.: Is it true that malignant melanoma is much more frequent in white animals than in pigmented animals of the same species?

DR. HARRY M. MARTIN (by invitation): Malignant melanomas seem to be more frequent in white and gray horses, but the skin of these animals is usually pigmented. However, malignant melanomas are not uncommon in pigmented animals. I recently saw this condition in 2 dark skinned animals (dogs).

DR. A. STRAUSS: Is the dosage for the young pig about equal to what would be used for the cow?

DR. MACK A. EMMERSON (by invitation): I have had no occasion to try the pig's tolerance to roentgen rays. I have a sow in the hospital now from which an 11½ pound (5,216 Gm.) actinomycotic tumor was removed. It is planned to irradiate the site of this lesion, and I may be able to answer this query later.

DR. A. STRAUSS: Dr. MacKee told me he had used young pigs in experimental work for determining skin dosage, since he found it nearest to human skin for this purpose.

DR. MACK A. EMMERSON (by invitation): I am glad to learn that. I consider all animals about the same—horse, cow and dog. Of course I have not run any actual test for skin tolerance alone, but the horses that have been treated seem to require the same amount of irradiation for discoloration of the hair as do the cow and the dog.

Parasites Affecting the Skin. Presented by DR. HARRY M. MARTIN (by invitation).

Microscopic and stereopticon slides are presented showing the following parasites or parasitic diseases:

1. *Mange*, in the ear of a rabbit. This condition is due to at least two species of mites. Large crusts may occlude the orifice.
2. *Scabies*, in a fox. This condition is rather common and is now a special concern of sportsmen.
3. *Demodectic mange*, in cow and dog
4. *Creeping eruption*.
5. *Mites*: (a) red mites of chickens, (b) larval form of *Trombicula*, commonly known as the chigger, (c) scabies mite, (d) sheep mite, (e) mite producing foot mange in horses, (f) mite causing mange in cats and (g) *Demodex folliculorum*.
6. *Pediculosis*: (a) chicken louse, (b) biting louse of the dog, (c) sucking louse of the dog, (d) common hog louse and (e) head louse of man, *Pediculus capitis*.
7. *Cat flea*.

Colored Motion Pictures of Some Common Cutaneous Diseases in Domesticated Animals with a Correlation of the Same Diseases in Man.
Presented by DR. J. V. KLAUDER.

Dermatitis Exfoliativa in a Horse.—The entire skin of the animal was involved. There was extensive desquamation composed of large scales. At places the skin was either thickened, edematous, moist and oozing or fissured. The animal had severe anemia. It died suddenly. From postmortem examination the apparent cause of death was intestinal obstruction.

Schorrhic Dermatitis in Cow and Calf.—In the cow the involvement was generalized. There were scattered irregularly shaped and ill defined patches in which the hair was absent or sparse. These areas were covered with fine greasy scales and presented little or no inflammation. The calf had considerably fewer

lesions which were sharply circumscribed and almost devoid of hair, the lesions resembled tinea. Microscopic examination of the scales from the lesions in both animals gave negative results for fungi. Recovery ensued in both animals after applications of 12 per cent sulfur and 8 per cent salicylic acid in petrolatum.

Cutaneous Lesions of Swine Erysipelas—One animal which recovered from the acute septicemic form of the infection presented on its back large, dry scaling patches, the desquamating remains of erythematous, purplish lesions that were present during the acute stage. The distal portions of both ears sloughed, which is not an uncommon occurrence after recovery from the acute stage of the infection. Such sloughing may include portions of the skin and also of the tail.



Fig 1—Lesions that characterize the mild form of swine erysipelas, so-called diamond skin disease

Concomitant arthritis, a notable symptom of the infection, was evidenced by swelling of the joints and by the stilty gait of the animal.

Cutaneous lesions which characterize the mild form of the infection in swine—so-called diamond skin disease—were shown. Such lesions, variable in size, were rounded, rectangular, quadrangular and rhomboidal. At places there were confluent lesions producing an outline unique in the domain of morphology of cutaneous diseases.

Syphiloid of the Cat—The animal presented on the inner surface of the upper lip a sharply circumscribed, elevated plaque, the surface of which was flat, moist and about 1.5 cm in diameter. The cervical lymph nodes were enlarged. This disease in cats is characterized by the presence of rounded or oval plaques that

favor the region of the genitalia, around the anus, on the abdomen or the inner surfaces of the hind legs, with enlargement of the regional lymph nodes. If the lesions disappear, they usually recur. The general health of the animal is eventually affected and death ensues. Clinically such a lesion has a striking resemblance to a hypertrophic mucous plaque of syphilis. Henry and Bory (*Ann. de dermat. et syph.* 10:104, 1929) compared the histologic appearance of the lesion with that of lymphoblastoma and the appearance of the enlarged lymph nodes with that of Hodgkin's disease.

Alopecia Arcata in a Dog.—There were a number of rounded spots devoid of hair, the skin of which was smooth and showed no pathologic alteration. The regions involved were the face and ears and part of the trunk. The disease was similar in appearance to that in man.

Sarcoma in a Dog.—A female bulldog aged 9 years presented on the right flank an infiltrated, hairless plaque about 5 by 3 cm. An amelanotic melanoma was diagnosed histologically. The animal was shown at a previous meeting of the society (*ARCH. DERMAT. & SYPH.* 37:688 [April] 1938). Despite roentgen irradiation and a minimum sulfur intake in the diet (*ARCH. DERMAT. & SYPH.* 38:160 [July] 1938) the animal died.

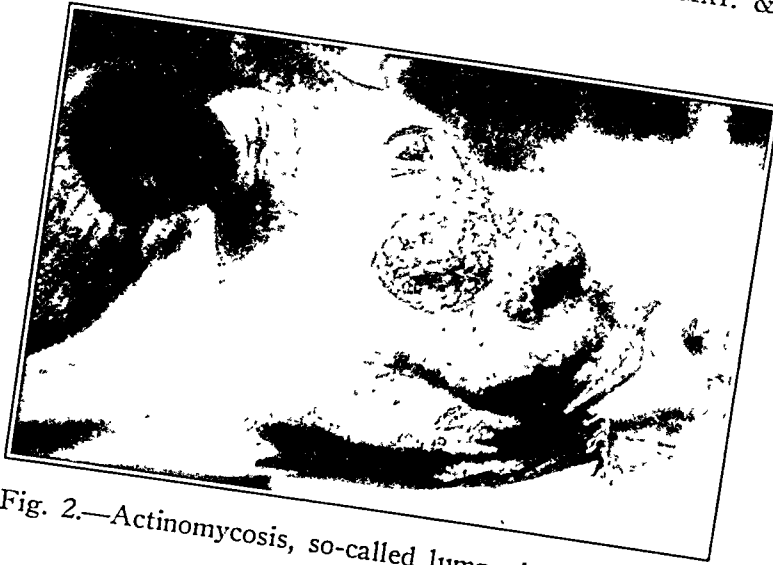


Fig. 2.—Actinomycosis, so-called lumpy jaw, in a cow.

Pyogenic Infections in Dogs.—A police dog presented on the face and legs sharply margined, round and oval erosive lesions, the surfaces of which were bright red, some of which were moist and oozing and others, slightly elevated and crusted. The animal had loss of appetite and diarrhea. The temperature was normal. The lesions resembled impetigo of Tilbury Fox.

On the abdomen and around the genitalia of a chow there were about six superficial erosive lesions which were circinate and gyrate in outline. Others were shaped like the letter S or the figure 8. Their surfaces were moist and oozing. The lesions resembled circinate lesions of impetigo seen in man.

Scattered over the trunk of a scotty there were a number of margined, rounded, crusted lesions which discharged seropurulent secretion.

A German shepherd dog presented on the abdomen around the genitalia a large, irregularly outlined, bright red patch with a moist, oozing surface. The lesion resembled intertrigo in man. There were similar but smaller lesions on the face and in the submaxillary region.

The following examples of eczematous lesions in different dogs were shown: circumscribed, rounded, dry, crusted lesions that resembled nummular eczema in man; moist, oozing patches of acute eczema, and chronic, thickened, lichenoid lesions of eczema. Examples of the following lesions were also shown: actinomycosis ("lumpy jaw" in cows), multiple cutaneous tumors in a colt and "red" or

the dry form of mange (*Demodex folliculorum*) in a dog. In this animal the entire skin was erythematous and covered with fine scales. There was partial loss of hair.

Dermatoses of Wild Animals in Captivity (with Lantern Slides) Presented by DR FRED D WEIDMAN

Pediculosis in Monkeys—Pediculosis is not common in monkeys, the parasites are seldom observed at necropsy. The scratching is due rather to dandruff or other conditions than to pediculi. Monkeys become lousy (1) when they do not have a cage mate whereby they mutually disinfest each other, or (2) when, as in the case of the spider monkey (*Ateles*), even with a cage mate, the thumb is such a small nubbin that it cannot be used to grasp the parasite. Morphologically the parasite is the same as that of man, but dark brown. Obviously it becomes increasingly difficult to distinguish between *Pediculus capitis* and *Pediculus corporis* in monkeys.

Scabies in Camels—An enzootic disease at the Philadelphia Zoo affected several camels, all of which died from exposure because their winter coats did not grow, owing to the ravages of the parasite. The crusting was so great that the condition compared with the Norwegian scabies of man.

The infestation was transmitted to 7 or 8 of the keepers and even to the truck driver who hauled away the carcasses. As is usual in cases of scabies of animal origin, the dermatitis transmitted to the human being responded promptly to treatment.

Scabies in Apes—A chimpanzee and an orang-utan yielded a parasite which was morphologically identical with that of man. Unlike the human condition, the scalp was affected, the fingers escaped. The keeper and his wife were infested (Weidman, F D. Certain Dermatoses of Monkeys and an Ape, *ARCH DERMAT & SYPH* 7:289 [March] 1923).

Creeping Eruption—Among the first hosts ever described for this intestinal parasite, *Ancylostoma braziliense*, was a lion in a menagerie in Calcutta. Bengalese cats and dogs, as well as 3 convicts, were parasitized (Weidman, F D. Distribution of *Uncinaria* Among the Lower Animals, *J Comp Path & Therap* 38:313 [Dec] 1915). The feces of man, too, are a reservoir for the dissemination of creeping eruption.

Fungous Infections—*Tinea circinata* was observed in young Barbary apes (*Macacus inuus*). There were extensive rings and patches of white scales on the head, the anterior surface of the arms and the abdomen. The centers were hairless. *Trichophyton gypsum* was isolated.

Ringworm in Chimpanzees (Pan Satyrus) and a Gorilla (Gorilla Gorilla)—This occurrence is common. The condition involves the inside of the thighs, the axillas and the abdomen. Small patches of papules have occurred on the cheek and on the flexor surfaces of the forearms. Lesions were grouped but not annular and apparently not itchy. *Trichophyton equinum* has been revealed in culture. Altogether I have observed 4 chimpanzees and 1 gorilla with dermatophytosis out of 11 animals examined and saw a chimpanzee in the Rome Zoological Garden which appeared, clinically at least, to have the condition. I have observed it in an experimental monkey in the laboratory, and there are other similar reports in the literature. At the Philadelphia Zoological Garden it does not appear to affect at all commonly the smaller monkeys, such animals as are likely to be used as pets.

However, the common rhesus (*Macaca mulatta*) was found affected by what was probably seborrheic dermatitis, as the scrapings exhibited budding organisms resembling *Pityrosporon ovale*. It involved the axillas and the sides of the chest and faded out into the surrounding skin. It was extremely superficial, with thick, scaly, yellowish to granular accumulations, and similar to dandruff except that it was distinctly yellow.

In an Indian rhinoceros (*Rhinoceros unicornis*) an exfoliative dermatitis was apparently due to a *pityrosporon* which was cultured and named *Pityrosporon*.

pachydermatis. Incidentally, Ciferri has adopted this strain—right or wrong—as the type species for the genus *Pityrosporon* (Ciferri, R., and Redaelli, P.: *Ann. mycologici* 27:261, 1929). Large, polygonal, barklike scales covered the entire body. An unidentified monilia was associated. I observed the same condition, but less extensive, in an African elephant in the Central Park Zoo in New York and saw a pityrosporon in the scrapings (Report of the Laboratory of the Museum of Comparative Pathology, Philadelphia Zoological Society, Philadelphia, 1925, p. 36).

Molluscum Contagiosum.—This condition was observed on the head of a wild turkey. Coalescent nodules the size of small marbles covered the comb, wattles and periorbital region.

"*Lentigo*" in *Chimpanzees* (*Pan Satyrus*).—This term is not exact, because the macules do not quite correspond to the lentigo of man. Normally some of these



Fig. 3.—Ringworm of groin and neck in a chimpanzee. Note scaliness of neck and upper part of chest.

animals are universally and diffusely "high yellow," especially females. In other chimpanzees the entire skin is black. In either event, the skin of the face is much paler. In 2 mulatto females, 5 and 7 years old, there were numerous black macules on the face, and in a third, 8 years old, a black patch in addition, on and around the nose. This may extend onto the mucosa of the lips. These lesions are blue black, like the blue nevus of man, and exhibit the histologic structure of the latter condition. In short, in chimpanzees, there is considerable variation in their pigmentary patterns. Orang-utans, which are red haired, do not exhibit the foregoing macular features. There is a promising field for studies of cutaneous pigmentation in these apes.

Erythema of the Face in Monkeys (*Macaca Suscata*).—Certain females exhibit this physiologic erythema at the menstrual period, and it is also occasionally observed in the male. Erythema and edema likewise occur around the buttocks and the vulva. It is most obvious in the case of baboons, in which the projections in females are sometimes huge. All of these conditions are evidently secondary sexual phenomena and may be suggestive in relation to acne vulgaris and other

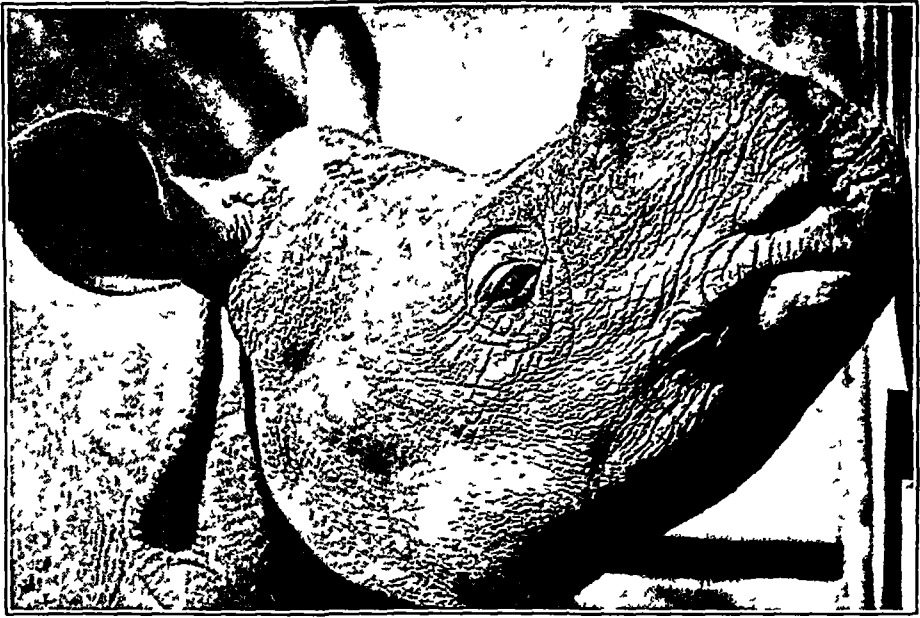


Fig 4—Exfoliative dermatitis in Indian rhinoceros (from the Philadelphia Zoological Garden) Predominating organism *P pachydermatis*, morphologically identical with the *P ovale* of human seborrheic dermatitis Observe the honey-comb-like pittings immediately in front of the ear

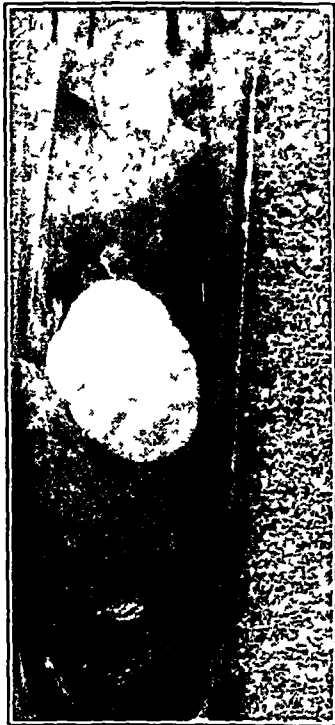


Fig 5—Culture of *P pachydermatis* (from rhinoceros with generalized exfoliative dermatitis)

dermatoses of man. Incidentally, at the London Zoological Gardens, monkeys have been spayed, whereupon the erythema failed to occur at the menstrual period; on administration of an estrogen the erythema was resumed during the menstrual period. The "sexual skin" of monkeys may be a suitable test object for studying the endocrinopathies (Zuckerman, S.: *Proc. Zool. Soc.*, London, 1930, pp. 702 and 718). An extreme grade of edema developed along the thighs of a female given large doses of solution of potassium arsenite (Weidman, F. D.: *Certain Dermatoses of Monkeys and an Ape*, *ARCH. DERMAT. & SYPH.* 7:289 [March] 1923).

DISCUSSION

DR. GEORGE M. LEWIS: I was interested in one practical point that was not brought out in regard to ringworm in animals. In dermatology fluorescence is made use of in discovering the extent of ringworm infection, and it is sometimes difficult to determine when cure takes place without resort to careful examination with the patient under the fluorescent rays. I wondered whether physicians here are in the habit of using such a light in the detection of ringworm in animals. Another question is in regard to ringworm in cats. It has been found to be easy to infect cats with ringworm, and one can almost at will transfer the infection to other cats, but when the cats reach a certain age it is impossible to go further with the work. At puberty, the infection apparently tends to die out in cats, as in man. I wonder whether this observation would apply also to dogs.

DR. REUBEN FRIEDMAN: The resemblance which the sarcoptic mite, of the dog and of the cat bears to the sarcoptic mite of human beings leads me to the observation that it was not until about two decades ago that, thanks to the work of Warburton (*Parasitology* 12:265, 1920) and others, it was determined that these mites found in various animals were not different species but merely different varieties of the same species, *Sarcoptes scabiei*. It was Buxton (*Parasitology* 13:114 and 146, 1921) who made the conclusive experiments with his studies on the horse. He compared the various parts of the external anatomy of the equine mite and the human mite and found there was little or no difference—certainly not enough to constitute a different species.

DEATH OF DR. PUSEY

As this issue was going to press, word was received of the death of Dr William Allen Pusey, Editor Emeritus, on August 29

Book Reviews

Handbook of Skin Diseases By Leon H Warren, M D Price, \$3 50 Pp 321 New York Paul B Hoeber, Inc (Medical Book Department of Harper & Brothers), 1940

The author of this small volume has gathered together information on two hundred and fifty-two cutaneous diseases and presents their essential features under the following headings etymology, synonyms and eponyms, essential nature, diagnostic features, differential diagnosis and treatment

The title itself prepares the reader for a compact and abbreviated outline of cutaneous disease, however, in some instances the form is almost too telegraphic The histologic descriptions are good for the most part, a few occupy relatively too much space at the expense of other aspects (especially diagnostic features and treatment), which might have been developed more fully

The diseases are presented in alphabetical order, which makes it an easy matter to find the desired subject In addition, the subjects are well indexed, the descriptive name as well as the proper name of an entity being given Not the least of many notable features is the chapter devoted to general principles of therapy, in which is found many time-honored formulas as well as physical means of treatment of the skin

This is a worth while volume which, because of its distinctive features, should fill a need of the student as well as of the specialist In the term *keratoderma palmaris et plantaris* the author's usual appreciation of Latin and Greek suffered a brief lapse

Reports on Medical Progress 1939 as Published in the New England Journal of Medicine Compiled and Edited by Robert N Nye, M D Price, \$5, cloth Pp 562 Boston Little, Brown & Company, 1940

The *New England Journal of Medicine* has, for many years, been publishing reports of progress in various branches of medicine The reports which appeared weekly during 1939 were somewhat different from previous ones Each review was limited to approximately 4,000 words The book consists of fifty-two chapters written by fifty-four authors covering the fields of general medicine, surgery and the various specialties Following each chapter is a list of references almost wholly limited to the years 1937 and 1938 There is an excellent index

Dermatologists will be particularly interested in the chapters on tuberculosis, the water-soluble and fat-soluble vitamins, physical therapy, cancer, allergic diseases, syphilis and dermatology

The desire of the editor that this volume "constitute a unique type of year book" has apparently been fulfilled It should be of definite value not only to the general practitioner but to the specialist who wishes to be informed of the recent advances in fields of medicine other than his own

CORRECTION

In the article by Dr Solomon Greenberg and Miss Ella D Mallozzi, "Experiments in Poison Ivy Sensitivity Effects of Specific Injections on the Level of Sensitivity to Quantitative Patch Tests and on Clinical Susceptibility," in the August issue (*ARCH DERMAT & SYPH* 42 290, 1940), the word "Negative" in the last line of table 2 on page 295 should read "Control," and the number "159" in the first line of the paragraph appearing immediately under table 2 should read "119"

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CULTURAL ASPECTS OF DERMATOLOGIC THOUGHT

PRESIDENT'S ADDRESS

FRANK CROZER KNOWLES, M.D.
PHILADELPHIA

Since the inauguration of this association in 1876, there have been numerous presidential addresses, and hundreds of papers have been read. It would seem that little if anything had been left unsaid. For years, however, various thoughts have been in my mind, at first vague and indefinite but becoming clearer and more rounded until they have become distinct convictions.

Teachers should realize that they can either make or mar the future of the potential leaders in medicine, including those in dermatology. Teaching should not be simply a routine. Each lecture should be the result of painstaking preparation and should be presented in such a way that it will hold the interest of the students. Whenever possible, a setting should be given to furnish a background for the discourse. For example, when dermatitis herpetiformis is discussed, one might give a short account of the life and activities of Dr. Louis A. Duhring. When the treatment of vascular nevus with solid carbon dioxide is described, one might give the highlights of the career of Dr. William Allen Pusey. When suggesting crude coal tar in the treatment of facial eczema of babies, Dr. Charles White might be referred to as the third professor of dermatology at Harvard, and it might be mentioned that his father, Dr. James White, inaugurated this specialty at that institution.

Lectures, if only a few, are necessary in the teaching of dermatology, a rather abstruse subject, to get the cobwebs out of the brains of the students. Personally, I have been much impressed with the thought that the students do not have actual contact with a sufficient number of dermatologic conditions. When the patients are presented in the amphitheater, only the students in the first few rows can see the significant details. Presentations may be made to small groups in classes in the wards, yet each student is in contact with only a few dermatologic entities. Therefore, an innovation has been made at the

Read at the Sixty-Third Annual Meeting of the American Dermatological Association, May 30, 1940, Colorado Springs, Colo.

Jefferson Medical College of Philadelphia Each week one third of the class attends student conferences, while the other two thirds examines dispensary patients arranged in separate rooms In this way, over a fifteen week period, each student will have had close contact with approximately 120 patients and will have had five one hour conferences for their discussion

The students also have the opportunity to study microscopic specimens pertaining to these cases, such as the animal and vegetable parasites, molds, fungi, cultures and histologic slides

Another point has occurred to me Are the students being instructed so that they will be able to make a clinical diagnosis, or is the making of a laboratory diagnosis being stressed too vigorously to the exclusion of the former? Scientific medicine is moving ahead so rapidly that the student may cease to realize that a clinical diagnosis must be made and then confirmed or invalidated by laboratory methods This point cannot be too strongly emphasized, otherwise certain eruptions with definite clinical characteristics either will not be diagnosed or will be improperly classified by the student who places exclusive reliance on the laboratory and none on what he sees

There could be no more graphic example than the clinical diagnosis of the late cutaneous eruptions of syphilis, because, as is well known, the positive results of laboratory tests of the blood help in only slightly over 80 per cent of these cases If the student's eye is not sufficiently trained and if he does not have a realization of the characteristic grouping and the destructive tendency, then the future practitioner of medicine will fail to diagnose the condition in from 15 to 20 per cent of the cases of this type

As to training the eye and the sense of color, some years ago on a rainy, murky day, a patient was presented to the students In addition to the eruption for which she was exhibited, the woman showed on her arm a curious, gyrated, festooned, weird-looking outbreak of variegated colors There was no thought on the part of any student as to the source of this curious outbreak The instructor took a wet towel and applied it to the outbreak, and it entirely disappeared The dyes from the moist shirt sleeve had stained the skin with the grotesque outbreak This emphasizes strongly that the student should be so trained that he knows the clinical appearance of at least the common cutaneous conditions

To go back again, students are potential leaders of the dermatologic thought of the future With this concept in view, they should be helped onward toward this leadership A few hours in their medical course, I believe, should be assigned to public speaking, training them to think while on their feet before an audience, and the proper methods of approach to and the preparation of a scientific paper

Dermatologists who have striven hard over a few or many years have their efforts crowned with success when they receive the accolade of membership in the American Dermatological Association. However, more is expected than that they should be leaders in this one sphere of endeavor. There should be a greater rounding out of the career rather than simply a superlative knowledge of one phase of life. A member of a scientific society should have knowledge in other fields, not only in science but in the fine arts as well. There should be added to the vocational science a certain amount of cultural education.

How can minds and thoughts of absolutely opposite lines mingle and entertain except by using culture as the bridge which unites members of diverse scientific societies?

Some months ago a group of physicians, most of them with diverse medical interests, made a journey of more than a hundred miles to confer with the state director of public health. In this group was an internationally known professor of medicine. Did this physician talk during the two hour journey entirely about his special line of endeavor? Instead, he led the discussion on the worthwhile modern novel and the classics of literature, both old and new, and the trip was a diversion rather than a continuation of daily endeavor.

Two of the most instructive and entertaining dinners I have ever attended consisted of not more than a dozen persons, both men and women, each a leader in a different line of endeavor. For entertainment, we had to meet on neutral ground, and that field had to be the fine arts.

There has never been a nation which has revered and worshipped knowledge and learning more than has China. By far the most popular god of Chinese literature is the demon-faced figure Kuei Hsing. Tradition says that he once lived on earth and attained, by his literary genius, the highest grade at the Emperor's official examinations but was refused the post to which he was entitled on account of his ugliness. In despair, he threw himself into the Yangtse River and was borne by the fish-dragon to the place which he now occupies in the firmament. The fish-dragon is his special attribute and is the emblem of literary perseverance and success. It is often used alone in symbolic decoration.

Notwithstanding the Chinese worship of knowledge, they believe in a rounding of character and culture and that a certain portion of time should be devoted to amusement. This is exemplified by the Chinese emblems of the four liberal accomplishments: painting, literature, music and checkers, which are represented on their porcelains, some hundreds of years old, by a picture scroll, books, a lute and a go (checker) board with a jar containing the pieces used in the game.

Should not, therefore, the Chinese point of view be a lesson that part of one's time should be devoted to entertainment and part to the

attainment of culture, while the greater portion should be intensively used in perfecting one's knowledge in a specialty?

One of my most revered and closest friends is a jurist. A suit was recently brought before his court as to whether certain chairs conformed to the Adam type. This judge remarked from the bench that at the time of Adam he did not believe there were any chairs made. As a leader of a learned profession, there should be sufficient general knowledge to distinguish the type of furniture made by the Adam brothers.

The difference between Tchaikowsky and Stokowski is not difficult, nor is the recognition of one or more of the outstanding compositions of Sibelius, the national musical genius of Finland. This speaks again for broader knowledge and vision.

A little study and contact will make one cognizant of and create a familiarity with the magnificent browns so characteristic of the portraiture of Rembrandt, the black background and the tapering fingers so often found in the oils of Van Dyck, the flattened and emaciated-looking profiles of El Greco and the feathery appearance of the foliage of the trees of Corot.

The most celebrated oriental rug extant, the Persian masterpiece of weaving of the sixteenth century, the "Holy Carpet of the Mosque at Ardebil," dated as of the year 946 A. H. (1568 A. D.), hangs in the Royal Victoria and Albert Museum, South Kensington, London. This rug, $34\frac{1}{2}$ by $17\frac{1}{2}$ feet (1,052 by 533 cm.), with about three hundred and twenty-five knots tied in each square inch, required over sixteen years to complete. An oriental rug is mentioned in an address of this character because of the following inscription woven into the texture:

I have no refuge in the world other than thy threshold,
My head has no protection other than thy porchway,
The work of the slave of this Holy Place

—Maksoud of Kashan, in the year 946 A. H.

A dermatologist should slave at his specialty because it is his life work, but he should not be a slave to it as this weaver was compelled to be.

Most of the world today is filled with unrest and chaos. What is really fine, the highest part of human nature—refinement and culture—hangs by a thread which can easily be broken for all time. It behooves members of this learned body to preserve that which is so well worth while.

What better precept or aspiration could one have than to take as one's aim in life the words of Vergil:

Sic itur ad astra

TREATMENT OF ACNE VULGARIS BY CRYO-THERAPY (SLUSH METHOD)

WILLIAM L. DOBES, M.D.

AND

HARRY KEIL, M.D.

NEW YORK

Solid carbon dioxide has been used as a therapeutic agent in dermatology for over a quarter of a century. In 1925 Giraudeau conceived the idea of applying a mixture of carbon dioxide "snow," acetone and sulfur in the form of a slush for the treatment of acne vulgaris and in subsequent communications described the details of the method as well as its rationale.¹ In recent years this type of therapy has been introduced in the American literature by Karp, Nieman and Lerner,² who reported rather striking results. In all the reports thus far issued no detailed attempt has been made to define the circumstances under which the slush method can be used to its best advantage in acne vulgaris, and the reader in perusing these papers is likely either to be skeptical or to gain the impression that this form of treatment can be applied with equal success in all forms of this disease.

During the past ten months we have had the opportunity to treat 115 patients with acne vulgaris and its sequelae. Of these 95 were observed long enough to afford us a fairly adequate idea as to the indications and contraindications of the slush treatment. As a result of this investigation it is our intention to attempt a more precise evaluation of this method, which we believe enjoys a definite place in therapeutics and yet has certain limitations.

TECHNIC

The technic has been fully described in the publications of Giraudeau and of Karp, Nieman and Lerner; yet a brief recapitulation seems in order, for we wish to introduce certain comments of a practical nature.

Solid carbon dioxide is placed in a mortar and by means of a pestle is ground to a fine powder. According to the aforementioned observers, about 10 per cent

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

1. Giraudeau: *Cryothérapie directe à l'aide d'un mélange de neige carbonique et d'acétone*, Bull. Soc. franç. de dermat. et syph. **35**:463, 1928; *La cure d'exfoliation par le mélange de neige carbonique, acétone et soufre dans l'acné*, *ibid.* **36**:654, 1929.

2. Karp, F. L.; Nieman, H. A., and Lerner, C.: *Cryotherapy for Acne and Its Scars*, Arch. Dermat. & Syph. **39**:995 (June) 1939.

precipitated sulfur is mixed with the "snow" and enough acetone is added to form a slush. In actual practice, however, much less sulfur may be added, with equally beneficial results, and in some instances the addition of this substance may be altogether abandoned. This mixture of slush is applied on a tampon of absorbent cotton, which is covered in turn with a square of gauze. It is now ready to be applied to the lesions. This procedure is carried out once or twice a week (in nearly all our cases it was done once weekly), and each area or lesion is treated with enough pressure for about half a second to produce blanching of the individual spots. After each application the sulfur, if incorporated in the slush, precipitates on the skin as a yellowish residue, which is allowed to remain for from fifteen to thirty minutes (average twenty minutes).

By this means a superficial freezing action is obtained, with the object of causing a certain amount of peeling. With greater experience, and depending on the type of lesion to be treated, the pressure exerted against the skin may be increased for the purpose of stimulating a greater inflammatory response, as in *acne indurata*. Because the tolerance of patients varies considerably with different textures of skin and complexions, it was our practice to begin with mild conservative treatments, increasing the amount of pressure until a satisfactory peeling was secured. On the average six blanching applications to each area treated once a week were required to obtain superficial exfoliation, in some instances as many as ten blanching applications were essential. Once exfoliation was obtained, it was observed to occur over the areas treated on the second or third day after the respective application of the slush, and the process was completed by the fifth or sixth day. It is likely, however, that in some instances peeling may occur sooner than we have mentioned.

Early in this investigation we tried to determine whether the sulfur added to the slush mixture was of special value. At the outset, therefore, we treated 10 patients with a mixture in which 10 per cent talcum powder was added instead of the sulfur. The peeling obtained and the response of the acne was far less satisfactory than when the slush contained precipitated sulfur, for in only 1 of the control group of 10 patients was the result satisfactory after four weekly treatments, whereas with the addition of precipitated sulfur the effects within a similar period of time were far more striking. It was therefore decided to use the substance in the subsequent routine treatment of our patients, except in certain conditions to be named later in this report. It is our belief that this is one of the best ways to apply sulfur in the treatment of *acne vulgaris*. In cases of *acne vulgaris* associated with pronounced oily skins, it was found advantageous to add acetone in excess so as to form a liquid layer over the slush, in this manner the drying effect on the skin was greater and the final results more satisfactory.

In occasional cases the application of slush may be accompanied by undesirable effects far out of proportion to what may be called the average or normal behavior of skin to solid carbon dioxide applied in this way. These unfavorable phenomena, which will be described, constitute evidence that caution must be exercised in instituting the treatment. In addition to these uncommon reactions, skin submitted to applications of slush exhibits the following normal behavior. During the application of the mixture there is often experienced a moderate burning sensation, which in the vast majority of the cases is transient and easily tolerated. After the removal of the powdery deposit on the skin, the treated surface is found to be moderately erythematous and in occasional instances slightly edematous. In the majority of cases the sensation of burning is greatly diminished or may altogether disappear, while in a few cases it may persist in a tolerable state for

several hours before complete disappearance. After a few treatments peeling occurs regularly. In some cases blistering may appear at points treated more intensively, and this is followed by crusting of a superficial type, with detachment of the crusts in from one to two weeks. In our observations such areas were never the sites of subsequent atrophy or scarring. As mild blistering was occasionally caused for therapeutic purposes, we do not consider it in itself an undesirable effect, except in rare instances in which it occurs as an evidence of abnormally diminished tolerance to the application of solid carbon dioxide. On the whole, we encountered in 115 cases but a half-dozen instances in which the reactions to this mixture constituted a real contraindication to its further use, and these exceptions will be described later.

EVALUATION OF THE ADJUVANT MEASURES

In introducing a new procedure in the treatment of acne vulgaris one must be cognizant of the pitfalls that confront one in the evaluation of results. It must be admitted that the fundamental cause of acne vulgaris is still unknown. The weight of evidence seems to point in the direction of an endocrine imbalance, but its precise mechanism remains speculative. In any event the results achieved thus far by the use of various endocrine preparations and other products presumably acting in a systemic manner have been regarded with considerable skepticism, and the best methods of therapy appear to be based on procedures involving only a direct action on the tissues, for example roentgen ray irradiation, ultraviolet irradiation and application of white lotion N. F. and various other topical remedies. The slush mixture is simply another such form of therapy.

In a recent communication Stokes and Sternberg³ stressed that there are apparently numerous factors capable of exerting a considerable influence on acne vulgaris, and apparently these factors are capable of inducing an exacerbation and the many unexplained variations in the normal course of this disease, with its periods of spontaneous improvement and recrudescences.

From the beginning of this investigation we began to encounter an occasional instance in which the secondary factors seemed to be of some importance, and it was decided to reinvestigate these points, with special reference to the question of diet and intestinal hygiene. There were a few patients requiring correction of secondary anemia, constipation and foci of infection. All the patients were requested not to use iodized salt, even though we have seen no clearcut examples in which acne vulgaris could be attributed definitely to this factor. Seborrhea of the scalp was an accessory factor of importance in some cases, and treatment was given when indicated.

3. Stokes, J. H., and Sternberg, T. H.: A Factor Analysis of the Acne Complex with Therapeutic Comment, *Arch. Dermat. & Syph.* 40:345 (Sept.) 1939.

In the majority of our cases the type of diet apparently had little influence on the course of the condition, except perhaps in an indirect way. There were 2 patients who would experience exacerbations when excessive carbohydrates were consumed. In an additional 9 patients there was a history of exacerbation of the acne vulgaris when fats were ingested in large quantities. Of these, 7 had a recurrence of their facial lesions when allowed to eat fatty foods again, even though they were given at the same time slush and other adjuvant measures. It was ascertained that 3 of the latter group and 4 others who were refractory to slush therapy were drinking large quantities of milk (1 to 2 quarts a day), and in these cases prohibition of milk seemed to be accompanied by a more favorable response to cryotherapy. So far as diet was concerned in its relation to our problem, our observations cannot be regarded as more significant than pointing to the belief that this is a secondary factor acting in some instances to produce intensification of acne vulgaris.

In 2 instances there seemed to be a relation to menstruation, for the cutaneous lesions became manifest shortly before each menstrual period. Gynecologic examination in these cases revealed no abnormalities. Slush treatment in these patients failed to produce a permanent response.

RESULTS

1 *Papulopustular Acne*.—Our data are based on observations made on a group of 69 patients with this form of acne. The number of applications of slush ranged from three for mild conditions to twenty-four for severe forms of the disease. On the average ten treatments were required before the condition of the skin of the face could be characterized as cured or as sufficiently improved so that cryotherapy could be stopped and local measures continued, including application of white lotion N F. Of the 69 patients 48 fell into this general category, and of the latter 32 were greatly improved and 16 were apparently cured. The past history of these 48 patients is interesting, for 8 had received previously a full course of roentgen ray irradiation, resulting in temporary improvement but followed by recurrence, for which they were now treated with slush, 9 had had roentgen ray irradiation (from five to sixteen treatments of 75 r each), with little or no improvement, 9 had had many treatments with the quartz mercury vapor glow lamp, with no improvement, 3 had also received treatments with a quartz mercury vapor glow lamp, with some amelioration but followed by recurrence, and the remaining 19 had been treated with the conventional local measures, such as application of white lotion, N F. It will be seen, then, that 17 patients had previously received roentgen ray irradiation, 12 had had irradiation from a quartz mercury vapor glow lamp, and the remaining 19 had had only topical therapy.

Of the 48 patients in whom the result could be considered as excellent, 11 had a recurrence within from two weeks to six months, though in the vast majority of these the exacerbation seemed to be considerably milder than the condition when first treated. Of the recurrences it is interesting that 3 patients among these had also had recrudescences after their previous roentgen ray irradiation treatments, despite adequate dosage. Of the 11 recurrences all but 3 responded rapidly to renewed treatment with the slush mixture. We are unable at present to furnish additional data on the further course of the disease in these patients. There were, in addition, 7 patients whose condition was but slightly improved; 6 were unimproved, and 8 were, for one or another reason, unable or unwilling to tolerate the treatment.

The incidence of successful results being 70 per cent (in 48 of 69 patients), this would on the surface seem to represent a considerable advance in therapeutics, especially since these patients had been treated previously by other methods. Yet this conclusion must be tempered somewhat in view of the following circumstances. While slush therapy proved an excellent adjuvant measure in certain cases, for the most part other accessory factors, as indicated, had also to be combated; in this respect this method is far inferior to roentgen ray irradiation. Whenever the latter is indicated in the management of the disease. That the effects of the slush treatments were purely local and often not permanent was indicated by the observation of recurrence in 11 of the group of 48 successfully treated patients, a minimal incidence of 25 per cent recurrences. It is true, in a degree, that so far as our material was concerned, the recurrences were generally milder than the original attack. In some patients, also, we observed that the skin would begin to break out at the end of the week, and it became necessary to control these lesions by advising the use of a mild white lotion.

As to the manner of action of slush on the pustules and papulopustules, it seems likely that the mixture acts in the following manner: (1) It causes freezing of the tissue, which is succeeded by an increased vascularity as the part thaws out, and (2) there is probably a mechanical drying effect on the pus and sebaceous matter due to a congealing action. We do not know whether freezing has any bactericidal properties in these cases. It is believed by some that the acetone in the mixture dissolves the sebum, permitting sulfur to be carried into the follicles, and it is further alleged that this deposition of sulfur has an inhibitory action on the sebaceous secretion; we are, however, uncertain that this is actually the case.

In order to clarify the situation further, we attempted to observe the effect of slush on the comedo, the elementary lesion of acne vulgaris. The comedo responded but slowly, if at all, to this type of treatment. Without adjuvant measures these lesions showed practically no improvement after a minimum of six weeks of applications of slush. It was

found best to have the comedos removed in the conventional manner just before the slush mixture was to be applied. In one instance, for example, the comedos kept recurring constantly, despite the preliminary extraction of them, in other cases it seemed the extraction of them, combined with applications of slush, apparently permitted the skin to remain free of comedos for a longer time. But we cannot draw this conclusion with any degree of confidence, as our material was insufficiently controlled in respect to this point. On the whole, then, no particular claims can be advanced regarding the efficacy of this method in the treatment of the elementary lesion of acne vulgaris, and the therapy of these often troublesome lesions resolves itself still into a matter of conventional routine measures.

2 Cystic Acne—The following data are based on a group of 24 patients with a condition that, for purposes of convenience, may be classified under two heads: (a) the soft, cystic type and (b) the hard, indurated type. The occurrence of transitions and combinations makes an absolute division difficult, and we have therefore been guided by what we considered to be the outstanding lesion in each case.

A Of the soft, cystic variety, the type characterized by more superficial pustular collections, there were 6 instances under our observation. The average number of applications of slush was twenty-one. Only 2 patients responded well, 3 responded poorly, if at all, and the remaining patient after receiving six applications of slush was referred for roentgen ray therapy in view of the poor result obtained by the former method. The last patient mentioned, from the beginning of his roentgen ray treatments, responded strikingly, and after receiving eight exposures of 75 r each, the condition of the skin was about 85 per cent improved. There can be no doubt that this was a definite instance in which roentgen ray therapy proved infinitely superior to cryotherapy. It may be noted, also, that in the group of 3 patients who gave similar unsatisfactory responses to a large number of treatments with the slush mixture, 1 patient had previously received twelve roentgen ray irradiations (75 r each), injections of chorionic gonadotropin (antuitrin S) and various local measures, and an additional fifty-one treatments with slush failed to influence the condition to any definite degree.

Whatever temporary results were achieved in this group could be attributed more reasonably to the use of such accessory measures as wet dressings, surgical incisions whenever essential and local care in the manner already mentioned.

B With cystic acne of the hard indurated type we observed 18 patients. The average number of applications of the slush mixture was twelve. Of this group 17 responded especially well to this form of treatment in combination with adjuvant measures, it is of interest to note that 7 of the patients had previously had roentgen ray irradiation.

tions, ranging from four to sixteen or more exposures, without substantial improvement. Only 1 patient responded poorly. In the group with successful results 4 had recurrences, which appeared about a month or more after discharge, but they responded rapidly to renewed treatment.

This type of so-called acne often proves one of the most troublesome to treat, owing to its obstinate, persistently recurrent character and the frequent association with hard keloid-like masses, which may proceed to the formation of large disfiguring scars. This is especially important when the face is affected. While in some instances the condition responds to roentgen ray irradiation, in a fairly large percentage it does not yield satisfactorily to this treatment modality and after a series of from six to eight or more exposures the patients become discouraged and begin to seek other methods of treatment. As in the papulopustular type of acne, the conclusions regarding the unusually high incidence of successful results in this group of cases must be tempered by acknowledging the importance of the adjuvant measures used. The most valuable accessory measures were the use of local wet dressings (solution of sulfurated lime N. F.) and surgical incision for the drainage of underlying purulent collections.

The application of the slush mixture was somewhat modified as compared with the technic used for the papulopustular type of acne. Attention was centered chiefly on the individual nodules, which received in some cases as many as twenty blanching applications with moderate pressure or were kept "frozen" for approximately thirty seconds by sliding the tampon over their surface, thus avoiding the adjacent normal skin. The latter procedure especially resulted in a severe inflammatory reaction, followed by peeling or even blistering; this was tolerated in all the cases submitted to this procedure and no scarring was observed in any instance. Under these circumstances the action of the slush seems to be twofold: (1) In some lesions absorption seemed to be favored, owing to the increased inflammatory reaction provoked by the thawing-out process, which happened chiefly in the relatively small lesions and was noted to occur in some instances after as few as three treatments; (2) in larger lesions the inflammatory reaction seemed to promote softening of the area treated, so that a linear incision could be made with a reasonable chance of securing adequate drainage of the enclosed pus; when incisions are made too early in the course, the observer is likely to find only indurated, edematous and bleeding tissue, without a definite localizable collection of pus.

In all likelihood the condition in these cases is related to the entity described by O'Leary and Kierland⁴ as pyoderma faciale and is also

4. O'Leary, P. A., and Kierland, R. R.: Pyoderma Faciale, Arch. Dermat. & Syph. 41:451 (March) 1940.

the counterpart of that regarded by Ramel, on insufficient grounds, as being a tuberculous condition, merely because the thick pus enclosed generally yields a sterile culture. It is our belief that the judicious use of slush, incision, wet dressings and local care, each employed according to their indication, offers in many cases a reasonable chance for control of this type of infection and increases the possibility of a better cosmetic outcome. On the whole, then, the successful results in this small group of cases can be attributed not to slush therapy alone but to its use in combination with other measures. We believe that the same principles would apply in the case of acne conglobata.

3 *Scars in Acne Vulgaris*—In 7 of the 69 patients exhibiting papulopustular acne there were scars which remained visible after the active lesions were gone. These were treated with from twelve to eighteen additional applications of slush in an effort to improve the appearance of the small cicatrices, but in our opinion the results were negligible. Similar treatment was carried out in 2 instances in which there was only scarring as the end stage of old healed acne, the final results were also unsatisfactory. An average period of from three to four months of such therapy seemed not to bring about any striking improvement or even sufficient progress to warrant further treatment. However, Karp is of the belief that at least eight months of applications of slush is essential before real improvement becomes manifest, while in the case of scars due to smallpox there are required from seventy-five to eighty treatments. In treating scars it is best to use a mixture composed of only acetone and solid carbon dioxide, sulfur is left out, as it may interfere with the particles of snow that are alleged theoretically to be retained by the peripheries of the cicatrices. It is for this reason that light rapid friction without pressure is advocated rather than the ordinary routine technic. It is believed that by this modification the edges of the scars retain small fragments of the slush while the depth remains untouched, thus rendering the central depression in the cicatrix relatively less deep in relation to the surrounding parts. The mechanism would then be analogous to what happens when the edges of scars are painted with phenol or trichloroacetic acid. If future observations indicate that this is more than a temporary deceptive result, the treatments with slush, no matter how extended a period of time may be necessary, would be indicated, for defects of this type may blight the existence of many a girl or woman. However, substantiation of these claims is needed, and the final results must be striking enough to overcome legitimate skepticism and permanent enough to offset criticism on the score of temporary deception.

4 *Acne Erconée des Jeunes Filles*—A patient with this condition (not included in the statistics) was successfully treated with the slush mixture, but we believe that this was accomplished chiefly because of

the psychologic effect which the method seemed to produce in this particular patient.

5. *Unfavorable Results.*—A. Two patients had an immediate urticarial whealing reaction accompanied by severe burning sensations over the treated areas. This persisted several hours. It is interesting that the application of solid carbon dioxide to the skin of the forearms of these patients also produced the same manifestations, and it is possible that the condition in these cases represents what is popularly known as "allergy to cold."

B. Severe edema of the face followed the application of slush in the case of a girl aged 17. The edema persisted for two days, even though

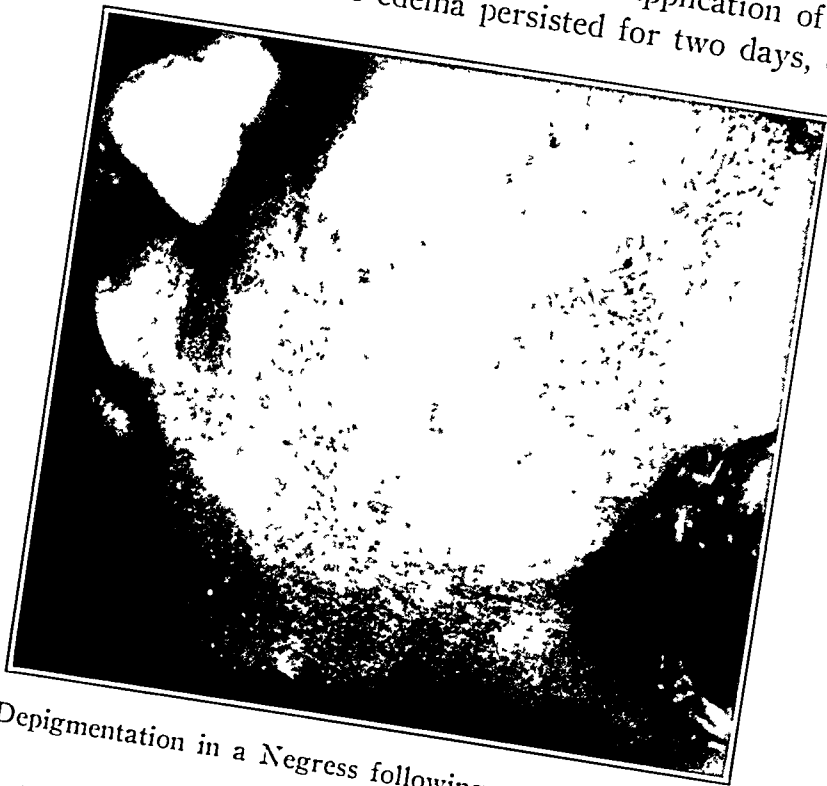


Fig. 1.—Depigmentation in a Negress following peeling with cryotherapy.

the treatment was not sufficiently intense to produce peeling. After this, the back was treated in a similar manner, and, indeed, strong peeling doses were subsequently given, without any untoward effects. On the other hand, a mild application of the slush to the skin of the face again produced a return of the unpleasant manifestations described.

C. Depigmentation of both cheeks and forehead of a young Negress followed the application of a peeling dose. The depigmentation persisted in its original state for three weeks, then required some six weeks for complete recovery to normal. In another Negress, whose chin was treated by this method, depigmentation lasted some six months, and the center of the lesion is slowly resuming its original pigmented state. It was also noted that patients having a deep tan would commonly show

a mottled blanching when the peeling reactions were intense. As solid carbon dioxide is often used in dermatologic practice for the purpose of blanching pigmented areas, for example, certain pigmented nevi, the aforementioned reaction is understandable, and for this reason we advise caution in the treatment of Negroes afflicted with acne or patients with a fresh sun tan. We are unable to state whether the depigmentation seen in dark-colored persons may not become permanent in some cases, nor are we certain about the converse, that is, whether hyperpigmentation may not occasionally occur in light-colored persons.⁵ These results suggest the use of this method, but with caution, in the treatment of

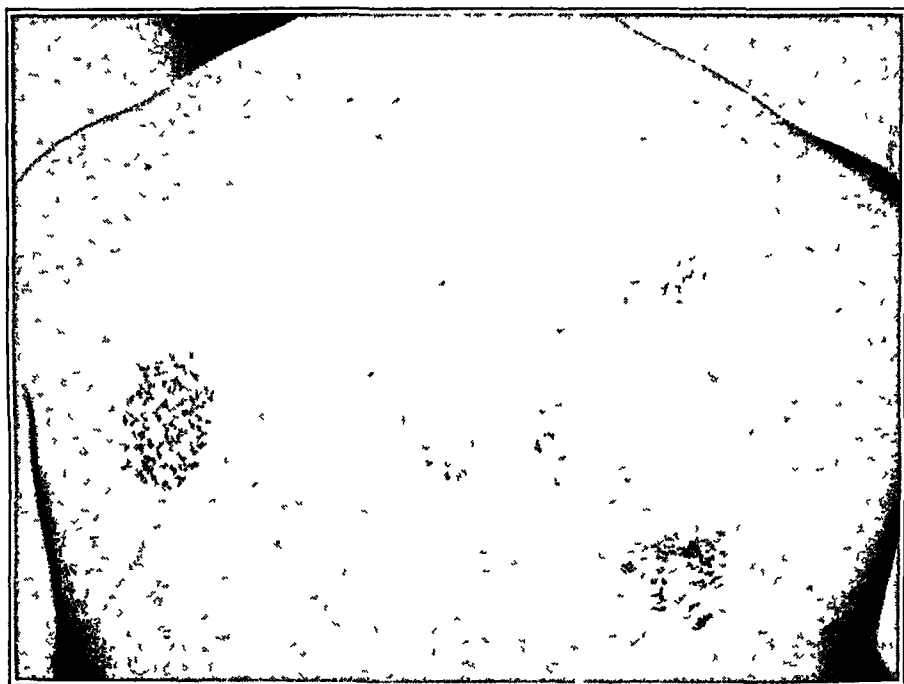


Fig 2—Purpuric mottling as result of application of a trial dose to the back of a man

chloasma and other pigmentary anomalies in which the pigmentation is attributable to an increased production of melanin in the epidermis.

D. Blotchy purpura-like patches appeared on the skin of a patient⁶ who received only a trial application of slush. These patches persisted for more than a month in their original state, and after a lapse of over six months areas of depigmentation and blotchy hyperpigmentation were still evident along the edges of the involved areas. It was found that

⁵ MacKee, G. M. Personal communication to the authors. Dr. MacKee stated that he had seen a young woman in whom pigmentation followed slush therapy and lasted for two or three months, and for this reason treatment had to be discontinued.

⁶ Botwinick, I. Unpublished data.

a mild application, without pressure, was instantly followed by a recurrence of the phenomenon. On the other hand, ordinary ice and cold water had no such effect. Whether this phenomenon is an example of unusual capillary fragility elicited by the application of solid carbon dioxide or of other ingredients contained in the slush mixture we are unable to state.

E. In a girl aged 23 previously treated with roentgen ray irradiation and topical remedies, there appeared a cropping out of pustules after the slightest applications of slush to the face. The patient, on the other hand, tolerated lotions containing sulfur but gave a history of having had recurrences of acneform pustules whenever the cold weather set in.

F. A few other patients would not tolerate the treatment, for it seemed to cause them unpleasant sensations.

As these observations have been made on the basis of a study of only 95 patients, it is likely that other investigators will meet with still other types of unpleasant local disturbances.

COMMENT

1. *Contraindications to the Use of Slush.*—A. No applications are to be made on patients showing smooth, elevated pigmented nevi or dark, so-called "beauty" spots devoid of hair, for in such instances one may be possibly concerned with potentially malignant lesions.⁷

B. Acne vulgaris in any form in the Negro appears to be a relative or absolute contraindication to the use of cryotherapy.

C. The immediate use of applications of slush after roentgen ray irradiation is regarded as contraindicated; about a month should be allowed to elapse before treatments with solid carbon dioxide are pursued.

D. A sun tan in patients constitutes a relative contraindication.

E. Those who show undue intolerance to the first application of slush are likely to prove intolerant to further treatments.

2. *Indications for Slush Therapy.*—The slush method of therapy is indicated for the following types of patients:

A. Patients who have not responded to adequate amounts of roentgen ray irradiation and other local measures.

B. Patients who have previously responded to the aforementioned measures and are afflicted with recurrences of variable degree and in whom it seems likely that further roentgen ray irradiation or topical therapy may be unavailing.

7. Traub, E. F., and Keil, H.: The "Common Mole": Its Clinicopathologic Relations and the Question of Malignant Degeneration. *Arch. Dermat. & Syph.* 41:214 (Feb.) 1940.

C Patients below the ages of 17 or 18, in conjunction with or independent of other local forms of treatment

D Patients with a dry skin, such patients forming a small definite group less likely to respond to either roentgen ray irradiation or other local measures, however, it must be admitted that there are no absolute rules in these cases (the slush may be applied to individual lesions)

E Patients with resistant acne indurata, especially of the hard deeper type, in whom the skin shows relatively little inflammatory reaction or an inflammatory action of a sluggish type, as a result of which there seems to be difficulty in resolving deeply seated purulent collections (slush therapy is an important adjuvant measure, having the advantage in the fact that applications can be made to individual areas)

F Patients who refuse roentgen ray therapy when it is clearly indicated (such refusals are generally made because of ill founded notions respecting the incidence of scarring and other effects, and the patient should be impressed that slush therapy promises less than would be expected from the average results achieved by roentgen ray irradiation)

G Patients with acne excoïée des jeunes filles (this method would seem to promise results in view of the opportunities to impress the patient psychologically)

H Patients with scars, provided that certain claims advanced can be substantiated

SUMMARY AND CONCLUSIONS

An attempt has been made to define the circumstances under which cryotherapy can be used to its best advantage in the treatment of various types of acne vulgaris

Cryotherapy is believed to be an important adjuvant measure for some types of acne, especially the papulopustular and the hard, indurated form

Slush therapy is in no sense a substitute for roentgen ray irradiation when the latter is indicated, in certain instances the use of slush may be substituted for roentgen ray irradiation under conditions that have been defined in this paper

Recurrences are encountered in at least 25 per cent of the cases, in some instances recurrences seem to be milder than the original condition, but that is not an easy matter to judge accurately

Its use in the cure or alleviation of scarring is not yet firmly established

Its use in the treatment of acne vulgaris seems to be promising, but no more than that can be said from our studies

The unpleasant phenomena and the contraindications in a few cases have been recorded

LATE SYPHILIS WITH RARE ORBITAL GUMMA

REPORT OF A CASE

HAROLD R. SNIDERMAN, M.D.
TORONTO, CANADA

AND
E. A. GLICKLICH, M.D.
CINCINNATI

Lesions involving the eyes or their external musculature are common in acquired and in congenital syphilis. They may present themselves as local lesions in the eyeball or orbit or may be local manifestations of intracranial infection.

Syphilitic involvements of the eye and adnexa most frequently seen¹ are: Primary chancre of the lid and conjunctiva; interstitial keratitis, congenital and acquired; iritis, in acquired and in congenital infection; choroiditis, focal and disseminated; retinitis; changes in the optic disk, without intracranial involvement; atrophy of the optic nerve; paralysis of the ocular nerves by a gummatous process in the orbit, basal syphilitic meningitis, cerebral gumma or syphilitic neuritis of the nerve trunks, and nuclear degeneration from disease of the supplying vessels. Gumma of the orbit is a rare condition.² It occurs in two forms:

- A. It may be a condition of the periosteum, especially in the upper and outer and the inner and lower quadrants of the orbit. Early it causes thickening of the structure and later necrosis, with possible breaking through the skin and formation of a sinus.
- B. A gumma deep in the orbit may give rise to symptoms from pressure on the optic nerve or cause symptoms similar to those caused by other orbital tumors, namely, exophthalmos and muscular paresis.

In the differential diagnosis of proptosis, the diagnosis of gumma of the orbit is one of the most difficult for ophthalmologists to make. The condition has been reported as showing unilateral and bilateral involvement, the onset not being simultaneous in each orbit. Fine³

From the Department of Ophthalmology and the Department of Dermatology and Syphilology, General Hospital, Cincinnati.

1. Moore, R. F.: Medical Ophthalmology, Philadelphia, P. Blakiston's Son & Co., 1925, p. 234.
2. Collins, E. T., and Mayou, M. S.: Pathology and Bacteriology of the Eye, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1925, p. 563.
3. Fine, M.: Gumma of the Orbit, Am. J. Ophth. 22:595, 1939.

reviewed the literature and found 24 cases of gumma of the orbit, to which he added 2 cases, one of a retrobulbar gumma and the second of a syphilitic periostitis of the orbit. Of the 24 cases, in only 5 was the condition bilateral. Kemp⁴ observed orbital syphilis in only 5 of 6,000 cases of syphilis at Johns Hopkins Hospital. Fine observed gumma of the orbit in only 2 among 40,000 patients seen in the ophthalmic clinic at Stanford University. According to Birch-Hirschfeld,⁵ syphilis of the orbit constitutes 0.01 per cent of all ocular disease. At the Cincinnati General Hospital, where 1,000 new cases of syphilis are observed each year, the case to be reported is the first of gumma of the orbit on record in the past twelve years.

Since the advent of antisyphilitic therapy, gummas of the orbit are becoming much more rare. There is usually a history of acquired or congenital syphilis of some years' duration or of inadequate treatment.

Frequently the first symptom is severe headache, worse at night, located in the eyeball or radiating to the forehead. A positive Wassermann reaction is important but is not always present. The proptosis which occurs is not reducible by pressure on the eyeball. Impairment of the function of one or more of the ocular muscles occurs, depending on the situation of the gumma, its size and the duration of the lesion. Roentgen examination is usually of no value. The response of the lesion to antisyphilitic therapy is diagnostic and dramatic.

REPORT OF CASE

A K., a 31 year old white woman, was admitted to the Cincinnati General Hospital in September 1938, with acute alcoholism and impending delirium tremens.

The patient gave a history of a lesion in her throat of one year's duration. Six months prior to admission she was struck with a fist on the left side of her face, and afterward she complained of weakness and numbness of this side of her face. Two months before admission she noticed a small sore on the bridge of her nose, and at the time of admission she complained of a purulent discharge and occasional hemorrhage from her left naris. One month before admission the left upper eyelid became weak, and at the time of admission she was unable to elevate it. She complained of pain in the left orbit.

In the past history there were no significant facts or any record of venereal disease.

The physical examination showed that she was acutely ill and under the influence of alcohol. Her pulse rate was 120, the respiratory rate 24, and the blood pressure 130 systolic and 100 diastolic. Her temperature was 100 F.

Examination of the eyes revealed. Uncorrected vision in the right eye was 20/30—1 and in the left eye 10/200. The right eye was normal in all respects. The pupil was round and 4 mm in diameter and reacted to light, in accommodation and consensually. The left upper lid was swollen, and there was com-

⁴ Kemp, J. E. Syphilis of the Orbit, *Arch. Dermat. & Syph.* 8: 165 (Aug.) 1923.

⁵ Birch-Hirschfeld, cited by Fine.³

plete ptosis. There was anesthesia of the upper lid in the region supplied by the supraorbital division of the ophthalmic branch of the fifth cranial nerve. The conjunctiva was clear. The cornea was clear and insensitive to cotton. There was no evidence of vascularization by slit lamp examination. The left pupil did not react to light or in accommodation; it was round and 5.5 mm. in diameter. In the fundus the retinal veins were slightly engorged. The arteries were normal in caliber. Tactile tension was normal. The eyeball was fixed in the primary position, with no ocular rotation in any direction (fig. 1, 1 and 2).

With an exophthalmometer there was 5 mm. of proptosis of the left eye (fig. 1, 2). The proptosis could not be reduced by pressure on the eyeball. There was no pulsation, and no bruit was audible over the left eye. A field of vision on the Ferree-Rand perimeter with a 3 mm. white test object revealed a concentric constriction of the nasal field for the left eye. The field for red with a 3 mm. target was decidedly constricted, and with a 3 mm. blue target the field of vision was within 5 degrees about the fixation point.

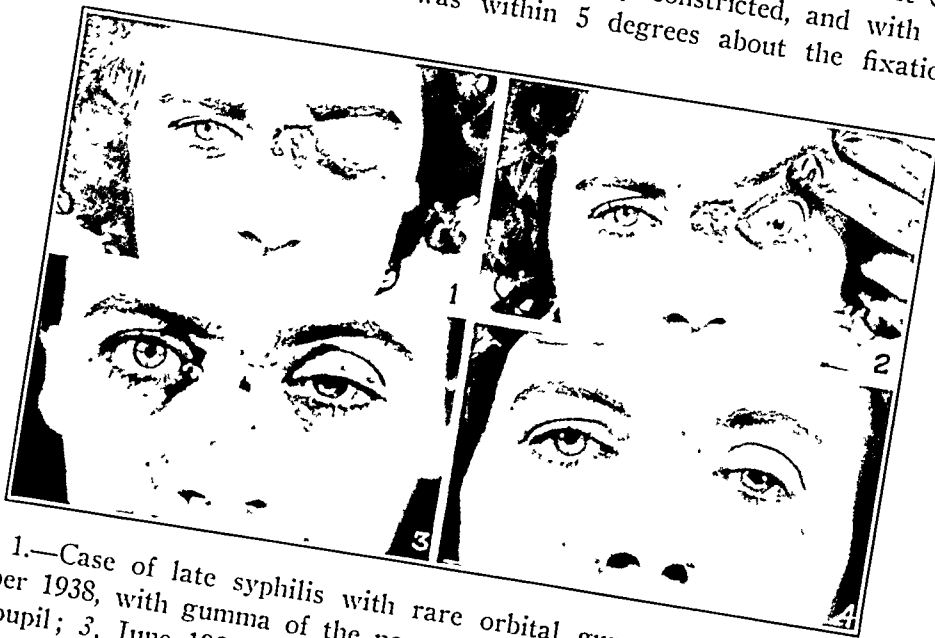


Fig. 1.—Case of late syphilis with rare orbital gumma. 1, on admission in September 1938, with gumma of the nose, complete ptosis and proptosis; 2, fixed dilated pupil; 3, June 1939, showing improvement of the ptosis and proptosis of the left eye and a small fistula into the nose; 4, January 1940, after a nasal plastic operation and intensive antisyphilitic therapy.

For the right eye the field of vision was normal for form and colors. A central field of vision on a Bjerrum screen at 1 meter with a 1 mm. white target revealed slight enlargement of the blind spot of Mariotte in the left eye.

The nasal examination revealed an ulceration of the mucosa of the cartilaginous septum, with a sanguinopurulent discharge. There was a hard granular mass extending down from the olfactory fissure, which obstructed the left nostril. Externally there was a deep ulcerated lesion, 2 by 2 cm., on the left side of the nasal bridge (fig. 1, 1), which was covered by a thick yellow scab. The edge of the ulcer was rough and undermined and bled easily when the scab was removed.

The examination of the mouth revealed an absence of upper teeth, carious lower teeth and poor oral hygiene. The uvula was absent, as was part of the soft palate on the left side of the midline. The edges were raw. There was a postpharyngeal mucopurulent discharge.

The remainder of the physical examination gave negative results

The following laboratory data were obtained Examination of the blood showed 12 Gm of hemoglobin per hundred cubic centimeters and 4,000,000 red blood cells and 9,000 white blood cells per cubic millimeter The differential count was normal

Urinalysis showed a 2 plus reaction for albumin and 4 to 5 white blood cells and 5 to 10 red blood cells per high power field

A cervical smear showed gram-negative intracellular diplococci

The cerebrospinal fluid was clear There was a slight increase in pressure The result of a Pandy test was negative There were 5 cells per cubic millimeter The Wassermann reaction was negative

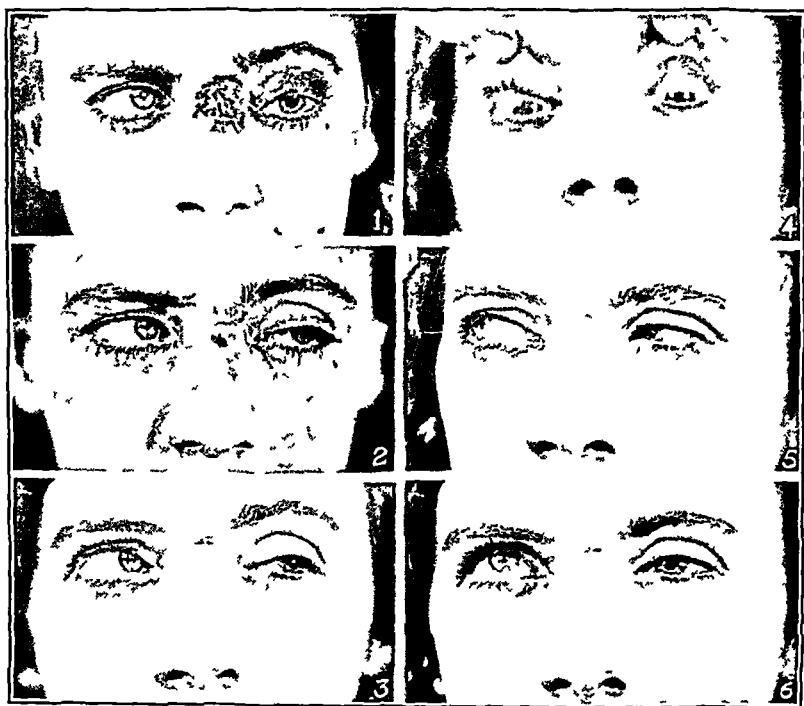


Fig 2—Movements of the muscles of the eye On looking to the left (1) with fixed left eyeball at time of admission, (2) nine months later and (3) fifteen months later January 1940, showing (4) improved movements of the left inferior rectus, (5) improved movements of the left internal rectus and (6) paresis of the left superior rectus muscle

A Kahn test of the blood gave a 2 plus reaction, and a Wassermann test, a 3 plus reaction

Roentgen ray examination (Dr B Felson) showed no significant abnormality of the orbit on the left side The optic foramens were normal The skull was essentially normal The bony nasal septum showed evidence of destruction in the central portion

From the aforementioned observations the diagnosis was (1) late syphilis, with (a) gumma of the nose, (b) gumma of the left orbit with total ophthalmoplegia, proptosis and involvement of the ophthalmic division of the fifth cranial nerve and (c) gumma of the uvula and soft palate, and also (2) gonorrheal endocervicitis

The patient was given intensive antisyphilitic therapy, which included the administration of neoarsphenamine, insoluble bismuth (bismuth subsalicylate) and potassium iodide.

In November, two months after the start of antisyphilitic therapy, there was a decrease in the proptosis of the left eye to 3 mm., but the ophthalmoplegia remained total. There was definite improvement in the nasal lesion. The granulating mass coming from the olfactory fissure had receded, and the septal ulceration was healing. The throat was completely healed.

In December the left upper lid had recovered some of its function and could be raised about 3 mm. The left globe showed returning rotations, the maximum rotation being in the field of the internal rectus, with the superior and inferior oblique muscles also active. The corneal sensation on the left was present but diminished.

In December the patient was discharged from the hospital and referred to the venereal disease clinic for further antisyphilitic therapy.

In June 1939 the uncorrected vision in the right eye was 20/20 and in the left eye 20/20—1. The left eye showed further improvement in the ptosis of the lid. The internal rectus muscle was normal. The external rectus, inferior and superior oblique and inferior rectus muscles were still paretic but greatly improved (fig. 2, 2). The superior rectus muscle showed little improvement and was paretic. The pupil was 3 mm. in diameter and did not react to light but reacted in accommodation and consensually. The cornea was sensitive to cotton. The proptosis was 1 mm. (fig. 1, 3).

There was a small discharging sinus on the nasal dorsum (fig. 1, 3), through which sequestrums were occasionally extruded. The patient was readmitted to the hospital, and a piece of skin full thickness from the postauricular region was grafted onto the bridge of the nose by Dr. S. Iglauder.

In January 1940, with the patient still getting antisyphilitic therapy, the changes in the left eye had become stationary. There was a decided improvement in all ocular rotations of the left eye with the exception of the field of the superior rectus muscle (fig. 2, 3, 4, 5 and 6). Her only complaint was diplopia on looking up and to the left and to the extreme left. The skin graft on the nose had closed up the fistula (fig. 2, 3). The healing was by primary intention. A roentgenogram of the orbit and optic foramina was essentially normal.

COMMENT

In the literature reviewed we have been unable to find another case of gummatous involvement of the orbit, nose and throat. The fact that photographic records of progress are available makes the case more interesting.

The elevated temperature at the time of admission suggested the possibility of an inflammatory cause for the proptosis, as did the foci of infection in the nose, but the presence of normal-appearing conjunctiva ruled this out.

Trauma to the left side of the face was no doubt a factor in the localization of the lesion and suggested the possibility of an arteriovenous aneurysm. This was the tentative diagnosis made at a neurologic conference. The fact that the eyeball was not replaceable by pressure

on the orbit, the absence of pulsation, bruit or any "buzzing" in the head and the presence of other late syphilitic lesions decided us against this diagnosis

As with other space-taking lesions in the orbit, the position of a lesion, whether inflammatory, malignant or vascular, causes displacement of the eye away from the lesion, and one at the apex of the orbit pushes the eye forward. This was the condition in our patient.

At the apex of the orbit are three openings through which important structures pass. The optic foramen carries the optic nerve and the ophthalmic artery. The superior orbital fissure transmits the ophthalmic vein, the third, fourth and sixth cranial nerves and the first branch of the fifth cranial nerve, supplying fibers to the skin of the upper eyelid and forehead. The sphenomaxillary orifice is the entrance for the second branch of the fifth cranial nerve, the sensory nerve to the lower lid and cheek.

In our case the lesion must have been in the region of the superior orbital fissure and pushing forward. All the nerves passing through this foramen were involved, and the slight dilatation of the veins in the left fundus suggested interference with the venous outflow of the eyeball. The anesthesia of the skin of the left upper lid pointed to involvement of the sensory nerve passing through this fissure.

The lesion must have encroached on the region of the optic foramen to explain the poor vision at the onset, along with some constriction of the nasal field of vision. This was probably slight, as the vision and field of vision returned to normal shortly after antisyphilitic therapy was started. Hotz⁶ reported a case of syphilitic orbital periostitis in which there were optic neuritis and almost complete loss of vision. After potassium iodide and mercury injections the vision returned to almost normal.

Carlin,⁷ in discussing lesions deep within the orbit or posterior to the orbit, stressed unilateral disturbances of the pupillary reaction to light. In our case the pupil remained fixed to light in spite of adequate antisyphilitic therapy.

Pressure on the orbital vessels explains the swelling of the left eyelids at the time of admission to the hospital. This receded as soon as treatment was started.

Roentgen ray examination repeatedly showed no abnormalities, it is usually of no value in the diagnosis of orbital gumma.

6 Hotz, F. C. A Case of Syphilitic Orbital Periostitis and Optic Neuritis in Which Vision Was Almost Extinguished but Completely Restored, *Ophth. Rec.* 12: 329, 1903.

7 Carlin, C., cited by Kemp.⁴

The skin graft filled in the fistula in the nose, and the lesion healed by primary intention, indicating that the patient was receiving adequate antisyphilitic therapy.

From the time of admission to the hospital to May 1940 the patient had 24 Gm. of neoarsphenamine and 5.85 Gm. of bismuth subsalicylate.

SUMMARY

A case of gumma of the orbit associated with multiple gummas of the nose and throat is described. The lesion in all probability was a periosteal gumma at the apex of the orbit. There was an excellent response to therapy and also to the plastic operation for the nasal fistula. The observations in the case are discussed with relation to the anatomy of the orbit.

Photographs were taken by Mr. J. B. Homan, assistant professor of Medical Art, Cincinnati Medical College.

BLACK HAIRY TONGUE

A REPORT OF THREE CASES

CHARLES BARRETT KENNEDY, M D

AND

JAMES K HOWLES, M D

NEW ORLEANS

Black hairy tongue (nigrities) is a hypertrophy which may involve all or part of the filiform papillae of the medial part of the dorsum of the tongue. It was first described by Rayer in 1835 under the term *discolorations pigmentanes*. In 1869 Raynaud reported several cases of it as a new entity and described the appearance of the tongue as a field of corn laid low by the wind.

Raynaud ascribed a parasitic cause to black hairy tongue, and this theory was confirmed by Laveau, Lancereaux and Dessois between 1876 and 1878. Gallois, Richter and Fereol, on the other hand, maintained that the presence of spores and mycelium was accidental rather than etiologic. Dessois, in 1878, and Gettheil, in 1889, unsuccessfully carried out inoculation experiments on their own tongues. Rayer, in his original description in 1835, mentioned the impossibility of inoculation and stated that spores morphologically similar to those present on black hairy tongue were present on normal tongues.¹

Weidman,² in 1928, reported a relation between black hairy tongue and trichomycosis. He considered the growth of the fungus on the tongue to be due to the fact that the development of the micro-organism is favored by the presence of keratin, which he found both on the hair of experimental monkeys and on the normal filiform papillae of the tongue of man. Thompson and Montgomery,³ in 1929, described an organism apparently related to the one found by Weidman and belonging to the classification Actinomyces.

It is generally agreed that the most common cause of black hairy tongue is some micro-organism, though there is still no unanimity of opinion as to what it is. Other possible causes include silver nitrate, chromic acid, syphilis, dyspepsia, tobacco, irradiation and various inflammatory lesions.

From the Department of Dermatology and Syphilology of the Louisiana State University School of Medicine and of the Charity Hospital of Louisiana.

1 Swinburne, G. Black Hairy Tongue, *J Laryng & Otol* **54** 386 (July) 1939.

2 Weidman, F. D. The Affinities Between Black Tongue and Trichomycosis, *Arch Dermat & Syph* **18** 647 (Nov) 1928.

3 Thompson, L., and Montgomery, H. An Organism Isolated from Two Cases of "Hairy Tongue," *J A M A* **93** 114 (July 13) 1929.

Extensive studies of black hairy tongue have been made by Heidingsfeld⁴ in 1910, Weidman² in 1928 and Swinburne¹ in 1939. The latter report is so complete in all details that there is no justification for a repetition of the study at this time, particularly as the author, from his personal observation of 16 cases and two pathologic specimens, spoke with an authority with which the subject had not previously been discussed.

Swinburne's observation of 15 of his 16 cases within fifteen months indicates that the disease is by no means as infrequent as it is generally supposed to be. Minor degrees, in his opinion, are likely to be overlooked. The disease occurs in adults, usually middle aged, and is considerably more common in males than in females. It is not usually painful but may be associated with a painful inflammatory or neoplastic lesion.

The extensive bacteriologic studies of Swinburne suggest that the microflora found in black hairy tongue should be regarded as coincidental rather than causal. He points out that the intimate association of mycelium in the folds of the epithelial layer is probably related to the chemical reaction. When the disease begins, it may be responsible for continued irritation, but there is no penetration of the tissues, and Swinburne's theory is that the condition is the result of metaplasia of the epithelium of the tips of the filiform papillae.

Histologic studies were possible in 2 of Swinburne's cases, which again is an unusual experience. The filaments of black hairy tongue were found to consist externally of a zone composed of mycelial elements and chains of cocci surrounding an inner mass of keratin. In many instances the center of the filament consisted entirely of flattened keratinized non-nucleated cells; in others there was an incomplete core of connective tissue covered by epithelial cells resembling those of the rete Malphigii. Since the filaments have none of the true characteristics of hair, Swinburne considered the term black hairy tongue to be a misnomer.

REPORT OF CASES

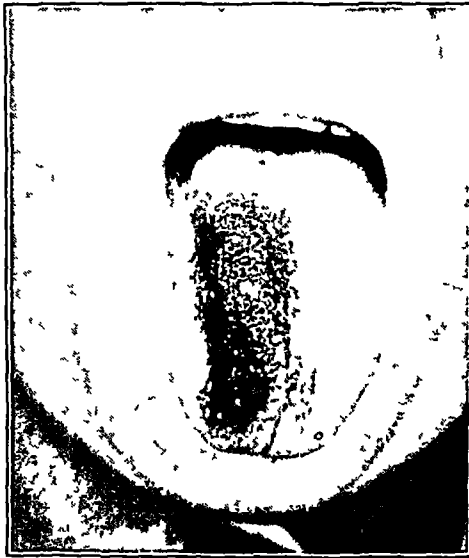
CASE 1.—A. G., a white railroad mechanic aged 40, had a black hairy growth on his tongue, accompanied by pain and swelling, for four months. He stated that the growth had first been observed a few days after he had cleaned an old tool shed and in the course of the work had laid his cigaret on a piece of wood covered with the same type of hairy growth which had later appeared on his tongue. He had brought the wood with him and was curious to know whether he had contracted his disease from it. The facts of his previous history were irrelevant.

Physical examination revealed no abnormality except for the tongue, the entire upper surface of which was coated with what seemed to be a thick, black hairy growth. The color was deepest in the center and faded to light brown at the

4. Heidingsfeld, M. L.: Hairy or Black Tongue, J. A. M. A. 55:2117 (Dec. 17) 1910.

edges The whole tongue was edematous, and the lower teeth left distinct impressions on the reddened lateral margins The right sublingual gland was swollen and the orifice reddened The insertion of a sound sufficiently dilated the orifice of the duct to permit the expression of a small calculus, followed by a profuse discharge of thick, clear mucoid material, after which the patient's discomfort was partially relieved

Urinalysis, study of the blood, a Wassermann test of the blood, examination of the stool and roentgenologic examination of the chest revealed no abnormalities Microscopic examination of scrapings from the tongue revealed keratinized filaments of epithelium and gram-positive bacilli, which could not, however, be identified as fungi A culture of the scrapings on Sabouraud medium revealed *Monilia albicans* and the same organism was cultured from the wood on which the patient had laid his cigaret The cultures were later examined by Dr Rhoda W Benham of New York, who reported the organism as *M. albicans* and regarded it as a contaminator



Black hairy tongue of four months' duration (case 1)

Almost every variety of therapy was tried, without much success Daily, biweekly and weekly scrapings of the tongue were followed by local applications of weak phenol solution, iodine, mercurochrome and silver nitrate A severe reaction occurred within two hours after the intradermal use of a 1:10 dilution of a vaccine prepared from scrapings from the tongue, reactions to successive intradermal injections were only slightly less severe, and continued vaccine therapy for many weeks resulted in no demonstrable benefit

At the end of five months of treatment an apparently spontaneous regression occurred, and the tongue became perfectly clean A slight amount of pain over the right sublingual gland, which had persisted throughout the five months, gradually disappeared shortly after the lingual condition cleared up

CASE 2—J G, an unemployed white man aged 33, applied for treatment for a black hairy growth which had been present on his tongue for two months With the previous case in mind we questioned the patient in detail, and he recollected that some time previously, while working in the yard, he had laid his cigaret on a piece of wood covered with some sort of black growth The wood in question had

been burned, but when he was shown the specimen in case 1, he immediately identified the black growth on it as similar to that on the wood on which he had laid his cigaret.

Physical examination showed no abnormality except that of the tongue, the appearance of which resembled that of the first patient's. There was a moderate amount of swelling, and the hairy growth was black in the center and faded to light brown at the periphery.

Urinalysis, study of the blood, a Wassermann test of the blood and examination of the stool revealed nothing abnormal. Microscopic examination and culture of the scrapings from the tongue revealed *M. albicans*, as in case 1.

A strongly positive reaction was observed within twenty-four hours after intradermal injection of 1 cc. of a 1:10 dilution of autogenous vaccine, and successive injections, even with greatly diluted solutions, produced such severe reactions that they had to be discontinued. The resulting malaise and lassitude, as in case 1, lasted for three days. Other treatment was not effective, and when the patient was last seen, sixteen months after his first visit, the condition of the tongue was unchanged.

CASE 3.—A. L., a white woman aged 23, had been under treatment for syphilis for three years. On a semiannual visit for a check-up (including a Wassermann test), she stated that for two weeks her tongue had been black. The results of examination were similar to those in the first 2 cases. No history of contact with wood could be obtained, and attempts to culture *M. albicans* failed, although the microscopic picture of the scrapings was similar to that seen in the other 2 cases. The tongue cleared up within four weeks without treatment.

SUMMARY

The first 2 cases reported are of interest chiefly because of the similarity of the histories and of the cultural findings. Both patients prior to the onset of the condition had laid their cigarets on wood covered with a black hairy growth similar to the growth which later appeared on their tongues. The same organism, *M. albicans*, was cultured from both tongues and was found on the specimen of wood produced by one of the patients. On Saboraud medium this organism exhibited a striking gross resemblance to the long black "hairs" found on both the wood and the tongue. In this connection it is interesting to recall that Plaut,⁵ who was the first to apply modern cultural technic to the study of disease caused by the group of organisms centering around *Syngasteria*, identified the mycelial form with *Monilia candida* Bonorden on decaying wood.

The third example of black hairy tongue occurred in a syphilitic subject and presented the same microscopic picture as in the first 2 cases, though attempts to culture *M. albicans* were unsuccessful. The condition regressed spontaneously, as in the first case. Therapeutic methods were unsuccessful in the first 2 cases, and vaccine therapy resulted in severe reactions.

5. Plaut, cited by Dodge, C. W.: *Medical Mycology: Fungous Diseases of Men and Other Mammals*, St. Louis, C. V. Mosby Company, 1935.

XERODERMA PIGMENTOSUM IN A NEGRESS

HOWARD KING, M D

AND

C M HAMILTON, M D

NASHVILLE, TENN

The rarity of xeroderma pigmentosum in Negroes should be of sufficient interest to justify the report of a case in a Negress aged 19. Three cases of xeroderma pigmentosum in a family of African Negroes were described by Loewenthal and Trowell¹ in 1938. In their report, of 5 children, aged 8, 7, 3½, 2½ and 1½ years, respectively, only 2 had escaped having the disease. The second and fifth were free of cutaneous manifestations. A striking similarity in the progress of the disease was present in all the cases. When the child was 1½ years old a pruritic pigmented eruption started on the face and soon spread to other parts of the body, resulting in pigmented and depigmented patches. Telangiectasis was not present. Ocular changes appeared soon after the onset, causing total blindness in the 2 older children and visual impairment in the youngest. Tumors of the tongue were observed in the 2 older children in the third year. An erosion which seemed to be epitheliomatous occurred on the lower lip of the oldest child in a later stage of the disease. The denial of consanguinity was not fully accepted.

A case of multiple epitheliomas and pigmentary dermatosis in a Negro boy reported by Hopkins and Van Studdiford² in 1934 may belong in this category. It appears that no other cases of a similar nature have been reported.

REPORT OF A CASE

In December 1937 a Negress aged 17 was referred to the outpatient department of Vanderbilt University Hospital by Dr. Thomas W. Knickerbocker, with a diagnosis of xeroderma pigmentosum. This diagnosis was accepted reluctantly, since the condition had never been seen in a Negro, a profound impression that photosensitization is considered an etiologic factor made it seem unreasonable for a dark, apparently full-blooded Negress to be a victim of this disease. The presence of hyperpigmentation, hyperkeratoses, ulceration of the nose, flaccid nevoid lesions on the face, white atrophic patches involving the exposed surfaces of the body and blindness should have been sufficient evidence for making a tentative diagnosis. Favorable comment by other dermatologists and, ultimately, the report of Loewenthal and Trowell, two months later, were substantial factors in arriving at this conclusion.

1 Loewenthal, L. J. A., and Trowell, H. C. Xeroderma Pigmentosum in African Negroes, *Brit J Dermat* 50:66 (Feb) 1938.

2 Hopkins, R., and Van Studdiford, M. T. Multiple Epitheliomas and Pigmentary Dermatoses in Negro Boy, *Arch Dermat & Syph* 29:408 (March) 1934.

At the age of 12 years she noted pigmented macules on the extensor surfaces of the forearms, which were not painful or pruritic. Many of the pigmented lesions were soon supplanted by depigmented spots. There was a gradual progression of this condition, and at the end of two years the arms, the face, the neck, the shoulders, the chest, the legs and the lower part of the thighs were affected



Fig. 1—Xeroderma pigmentosum in a full-blooded Negress.

in a similar manner. The palms, the soles, the upper parts of the thighs and the lower part of the trunk were never affected. During the next five years the lesions did not spread so rapidly, but a gradual increase in hyperpigmentation and a decided increase in depigmented patches became prominent features. Hyperkeratosis developed in all of the affected regions, but more distinctly on the face. Bleeding ulcerations of the nose began to occur more than two years ago, and in the meantime others continued to appear on various parts of the face, the chest and the legs. Both pedunculated and sessile nevoid excrescences of the face have

required removal at various intervals. Recently a large cornu cutaneum of the left upper eyelid was destroyed by electrocoagulation. Telangiectases were present in the atrophic areas, but they were not outstanding.

Within the last few months a large, nodular, fungating lesion with a foul odor appeared on the inner surface of the right leg. A small nodule of similar con-

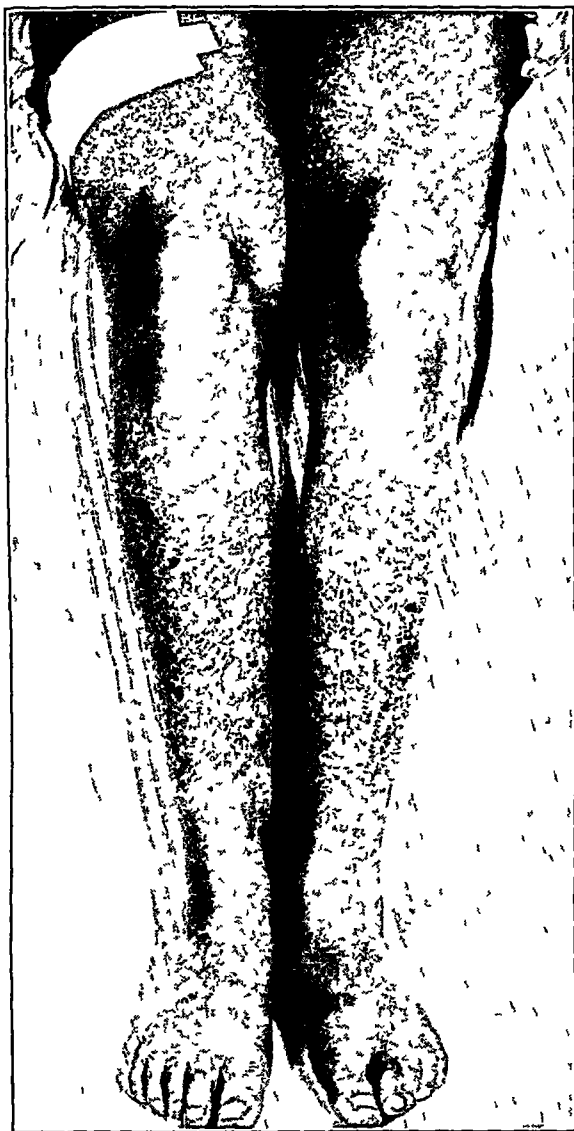


Fig 2—Xeroderma pigmentosum in a full-blooded Negress

sistency appeared on the posterior surface of the left leg. Both lesions had the gross appearance of rapidly growing epitheliomas, but this interpretation was not confirmed by biopsy, which seemed inadvisable in the presence of infection and since radiation therapy was elected as the method of treatment.

At the age of 13 her vision began to fail, first in the left eye and later in the right. The blindness was progressive, until at the time of examination light

was barely perceptible. There were extensive areas of scar formation on the cornea, keratitis and atrophy of the conjunctivas of both eyes.

The general health was always good, and at the time of examination the patient was well nourished, weighing 117 pounds (53 Kg.). Three brothers, 12, 14 and 16 years of age had very dark skins and were free of this condition. Her mother and father were cousins, had good health and appeared to be full-blooded

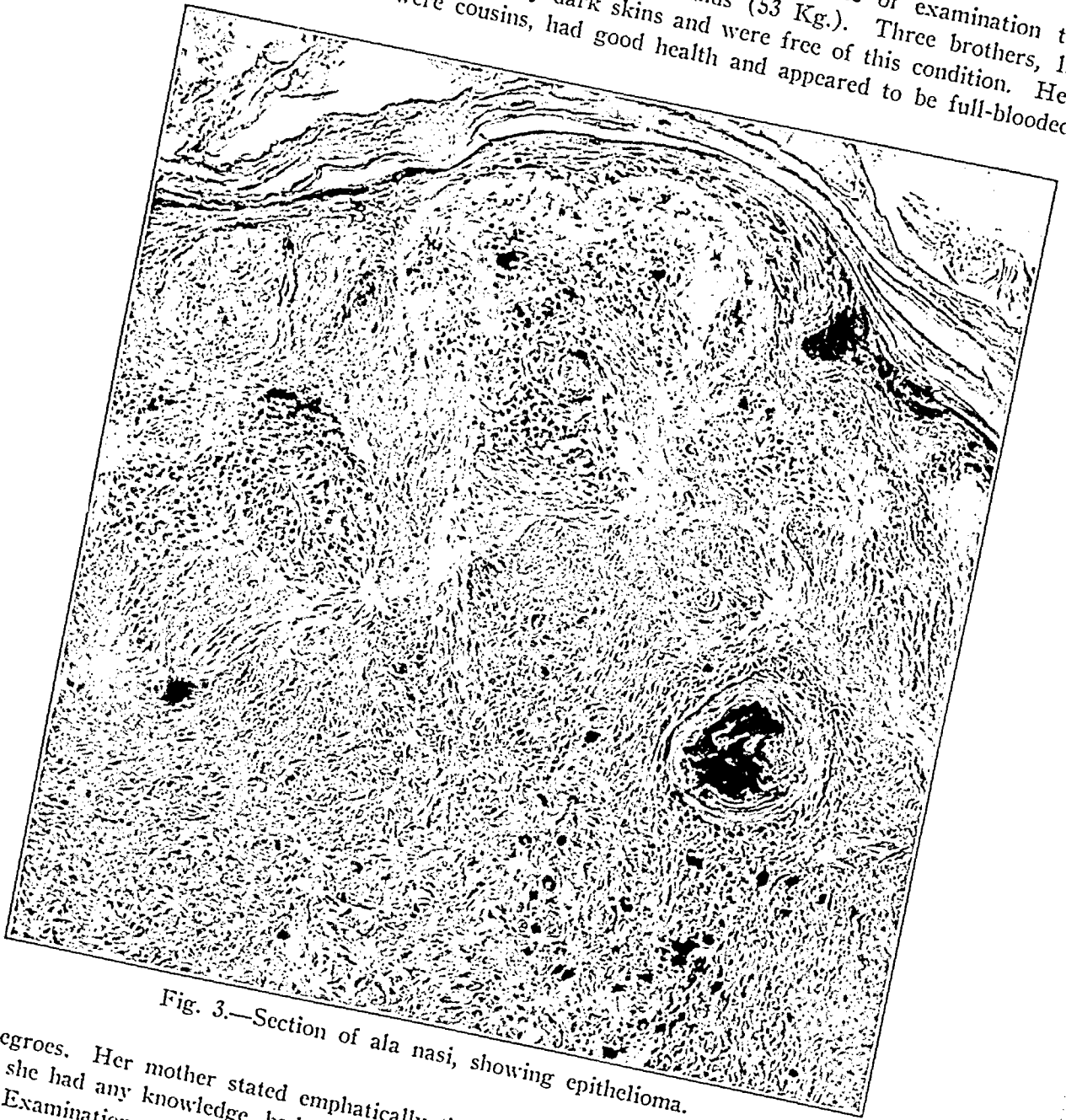


Fig. 3.—Section of ala nasi, showing epithelioma.

Negroes. Her mother stated emphatically that all the grandparents, as far back as she had any knowledge, had very dark complexions.

Examination of the blood showed 4,490,000 erythrocytes and 6,050 leukocytes per cubic millimeter and 12.6 Gm. of hemoglobin per hundred cubic centimeters of blood. The differential count showed: 61 per cent polymorphonuclear leukocytes, 33 per cent lymphocytes, 3 per cent eosinophils, 3 per cent large monocytes and transitionals and no basophils.

A Wassermann test of the blood and urinalysis gave negative results. The basal metabolic rate was —17 per cent.

A small, pea-sized lesion excised from the ala of the nose on Feb 28, 1940, was referred to Dr Herman Spitz for microscopic study, and his report follows

"The specimen is dark, lobulated and rather firm. The epidermis is thin and covered by cornified epithelium, which is thickest in the folds between the lobules. The stratum germinativum is smooth and pigmented. At variable distances rete pegs appear, which are usually elongated and branching in the lower portions. A few of them contain Perles's bodies. More frequently the rete pegs terminate in broad branching masses of small, round, uniformly stained cells. Similar masses of cells are found throughout the corium and in the deeper portions of the section



Fig 4—Section of pigmented macule on dorsal surface of forearm, showing hyperkeratosis, irregularity and prolongation of rete pegs, dilatation of blood vessels, perivascular infiltration, edema of cutis and numerous chromatophores in the upper portion of the cutis (hematoxylin and eosin stain, $\times 100$)

Both fine and coarse particles of pigment are scattered throughout. Congested, thin-walled vascular spaces are present, mostly in the superficial areas. Only an occasional mitotic nucleus is observed, but considerable round cell infiltration is seen in the connective tissue stroma. The section shows carcinomatous tissue of both the basal cell and the squamous cell variety."

Additional comment on the examination of biopsy material was made by Dr R N Buchanan, of the department of dermatology, Massachusetts General Hospital

"Specimens for histologic examination have been secured from an ulceration on the nose, from a pedunculated lesion on the forehead and from pigmented

spots on the face and forearm. Sections of these specimens show a variety of changes, consisting of hyperkeratosis, irregular proliferation and prolongation of the rete ridges. At places the epidermis is thin and atrophic, with the atrophy being most marked in the prickle cell layer. Near the ulceration the epidermis shows degenerative changes with pyknotic and fragmented nuclei. There is an abundance of pigment in the cells of the basal layer of the epidermis, and in certain

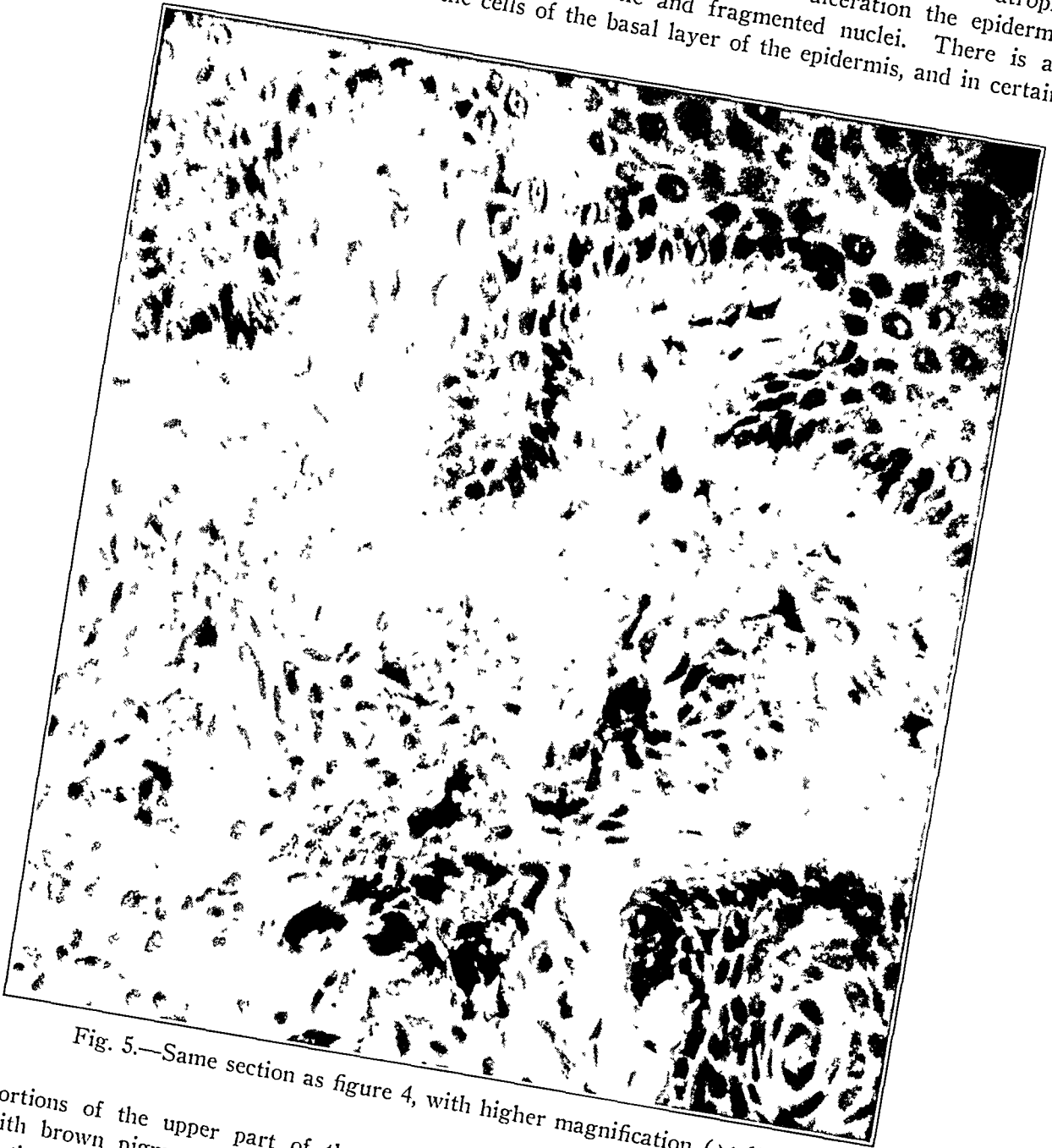


Fig. 5.—Same section as figure 4, with higher magnification ($\times 600$).

portions of the upper part of the cutis large, irregular chromatophores loaded with brown pigment are numerous. Some edema of the corium and dilatation of the blood vessels in the cutis are present, and there is a moderate round cell perivascular infiltration. The features are consistent with the pathologic changes seen in xeroderma pigmentosum, as described by Montgomery and Reuter.³

3. Montgomery, H., and Reuter, M. J.: Xeroderma Pigmentosum: Report of Mild Case with Histopathologic Studies, Arch. Dermat. & Syph. **26**:256 (Aug.) 1932.

TREATMENT OF DERMATOPHYTOSIS PEDIS WITH MEDICATED INSOLES

MORTON SELDOWITZ, M D

BROOKLYN

In recent years dermatophytosis pedis has been receiving major consideration because of its rapid and universal spread and its frequent resistance to prophylaxis and treatment. Morginson¹ estimated that 10 per cent of all cutaneous infections treated today are due to fungi. He stated that in a recent survey at the University of Pennsylvania 59.7 per cent of 1,073 students examined were found to be infected. Legge, Bonar and Templeton² conducted a similar survey at the University of California and found that of 1,000 freshmen entering the university, 51.5 per cent were infected, at the end of the first semester this number was increased to 78.6 per cent.

A review of the literature on the treatment of dermatophytosis pedis reveals a variety of therapeutic procedures, with many variables in the results obtained. In their study conducted at the University of California over many years, Legge, Bonar and Templeton³ attempted to establish the efficacy of a number of therapeutic agents, which included 30 per cent sulfurous acid in glycerin, 1 per cent thymol in glycerin, Castellani's solution, a 10 per cent ointment of benzyl peroxide, tincture of iodine and glycerin in equal parts, a 10 per cent solution of sodium thiosulfate, compound ointment of benzoic acid N F (Whitfield's ointment), compound ointment of benzoic acid N F with 1.5 per cent thymol, 4 per cent chrysarobin in chloroform, a pine oil soap solution, 5 per cent gentian violet in alcohol, 5 per cent aqueous solution of mercurochrome, 10 per cent ointment of copper oleate and ultraviolet irradiation from a quartz mercury vapor glow lamp with a special applicator. Their best results were obtained with compound ointment of benzoic acid N F containing 1.5 per cent thymol. They obtained complete recovery in 29 per cent of their patients thus treated, and another 35 per cent showed at least 50 per cent clinical improvement—this giving

The treated inner soles employed in this investigation were obtained from the Climax Rubber Company, which has the patent rights.

1 Morginson, W J. Fungus Infection of Hands and Feet, Illinois M J 70 371-376 (Oct) 1936

2 Legge, R T, Bonar, L, and Templeton, H J. Epidermomycosis at the University of California, Arch Dermat & Syph 27 72-74 (Jan) 1933

3 Legge, R T, Bonar, L, and Templeton, H J. Epidermomycosis at the University of California, Arch Dermat & Syph 29 521-525 (April) 1934

what the authors termed satisfactory results in 64 per cent of their patients treated by that agent. Six per cent of their patients showed definite evidence of irritation. The highest percentage of cures was obtained with their tincture of iodine and glycerin. They obtained recovery in 31.7 per cent of patients treated with this agent and satisfactory improvement in another 24.6 per cent. About 2 per cent showed evidence of irritation.

The treatment of dermatophytosis of the feet should be based on a comprehensive knowledge of the many problems arising in this type of infection. It has been established that the causative fungi frequently lead a prolonged and hardy life, with a resting spore age of indefinite duration and latent virulency. Parkhurst⁴ stated that its spores can survive as long as twenty-five years on glassware. The fungus, with its predilection for the interdigital spaces, causes local irritation and inflammation, maceration of the skin and increased perspiration. Frequently an objectionable odor accompanies the infection, due to the putrefaction of the excessive perspiration and to the macerated epidermis. Because of the nature of the causative fungus, treatment must necessarily be constant and prolonged. The employment of strong antiseptics is, as a rule, contraindicated, because frequently they have no effect on the mycelia and often produce local injury to the skin. Souter⁵ and others advocated an ideal, hypothetical therapeutic agent which should possess the following characteristics: (1) ease of application, (2) fungicidal or at least fungistatic action, (3) the ability to penetrate to the fungus in normal or pathologically altered structure of the epidermis, (4) nonirritation of the skin, (5) the ability to lessen perspiration and to prevent its putrefaction and (6) the ability to deodorize.

FUNGISTATIC EFFECTS OF MEDICATED INSOLES

Recently Kahn and Carroll⁶ have demonstrated that rubber containing 8-hydroxyquinoline was bacteriostatic for many organisms, particularly the staphylococcus. I have demonstrated the practical application of this finding in the treatment of impetigo contagiosa.⁷ On further experimentation Carroll and his co-workers found that the addition of parachlorometaxylenol and chlorthymol to the rubber base combination imparted definite fungistatic properties to this substance. A method was then devised to render an ordinary leather insole fungi-

4. Parkhurst, H. J.: Treatment of Ringworm of the Feet, Ohio State M. J. **34**:288-291 (March) 1938.

5. Souter, J. C.: A Clinical Note on Fungus Infection of the Feet, Proc. Roy. Soc. Med. **30**:1107-1116 (April) 1927.

6. Kahn, M. C., and Carroll, R.: Personal communication to the author.

7. Seldowitz, M.: Treatment of Impetigo Contagiosa with Rubber Containing 8-Hydroxyquinoline, Am. J. Dis. Child. **59**:67-75 (Jan.) 1940.

static The air in the pores of the leather was evacuated and replaced with rubber This rubber was then impregnated with 8-hydroxyquinoline parachlorometaxylenol and chlorthymol

It was found that this leather-chemical compound was fungistatic for *Trichophyton interdigitale*, *Trichophyton rosaceum*, *Trichophyton rubrum* The following experiments illustrate the fungistatic effects of these medicated insoles on *T. interdigitale* This fungus was chosen for demonstration because it is the most frequent cause of dermatophytosis pedis The medium consisted of Sabouraud dextrose agar (peptone 1 per cent, dextrose 4 per cent and agar 1.5 per cent with the p_H adjusted to 5.8), 20 cc in a glass top Petri dish The inoculum consisted of 1 cc of a heavy fresh suspension of spores of the organisms The material to be tested was washed with a sterile cotton swab and then with sterile distilled water and cut into 1 cm squares The squares were blotted on sterile filter paper and applied to the surface of the hardened inoculated agar plate for specific periods and then the plate was incubated at room temperature for seven days A 1 cm square of the medicated insole was first placed in contact with the inoculated medium for periods of one, five and fifteen minutes respectively The area of inhibition of growth for a one minute exposure was 1.6 cm, for a five minute exposure 3.6 cm and for a fifteen minute exposure 5 cm It is interesting to note that, though the 1 cm square of the insole was fixed on the inoculated agar plate, the area of inhibition of growth extended well beyond this area This would indicate that the medicated insole throws off a fungistatic substance which diffuses into the medium at some distance from its original site There was apparently no effect on the medium itself (fig. 1 a) On exposure of the inoculated agar to the 1 cm square of the leather-chemical compound for half an hour, the area of inhibition was increased to 5.6 cm A full hour exposure increased this area of inhibition to 9.1 cm, as indicated in figure 1 b In the final test the exposure was increased to six hours, and the inoculated agar plate was then incubated for the usual seven days at room temperature This procedure resulted in complete inhibition of growth of the fungus (fig. 1 c)

As a control, three pieces of an untreated leather insole, each 1 cm square, were placed clockwise on the inoculated medium for one hour, six hours and seven days, respectively The medium was incubated at room temperature for seven days This procedure resulted in a healthy growth of the fungus over the entire agar plate, as demonstrated in figure 2 The piece of untreated leather insole which had been in contact for a period of seven days is readily discernible and is surrounded by a dense growth of the *T. interdigitale*

MYCOLOGIC STUDY OF CLINICAL CASES

In an attempt to determine whether the previously described investigations could have a practical therapeutic application, a fifteen month study of dermatophytosis pedis was instituted at the Brooklyn Hebrew Orphan Asylum. Of a total of 327 inmates in the institution, 125,

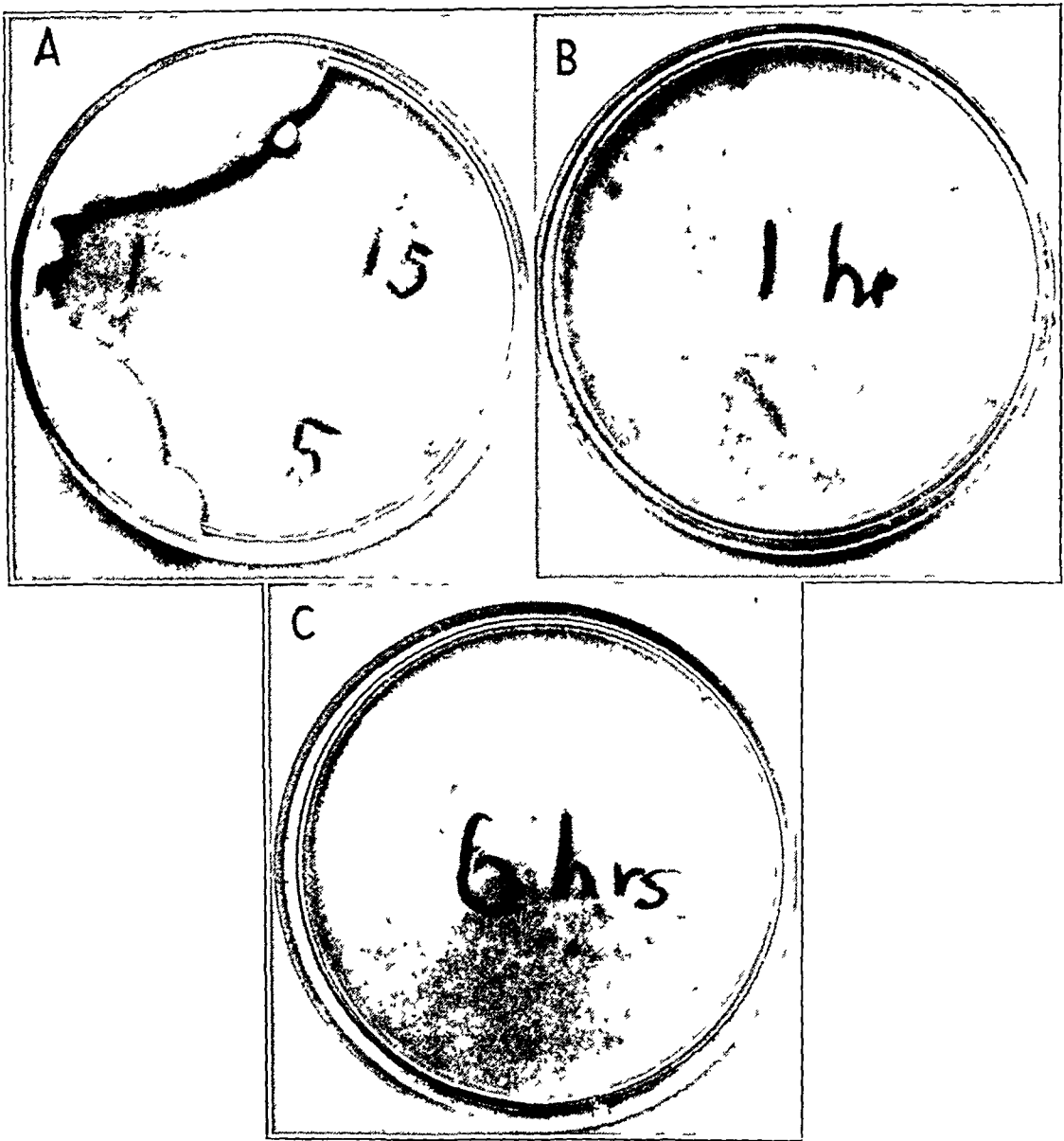


Fig. 1.—Effect of 1 square centimeter of the insole on medium heavily inoculated with *T. interdigitale*. *A*, numbers denote minutes of exposure. Note the areas of inhibition of growth. *B*, note larger area of inhibition of growth on increasing the exposure to one hour. *C*, after increasing the exposure to six hours, the zone of inhibition is complete and extends to the periphery of the plate. There has been no apparent effect on the medium.

or 38 per cent, were found to have clinical evidence of infection. The incidence was equal for boys and girls, the environment for both groups

being practically alike. Each clinically infected patient was subjected to a mycologic study. The lesions were washed with 70 per cent alcohol, and the outer margins were scraped with a dull, sterile scalpel. The first scrapings were discarded, but the deeper scrapings were placed on sterile glass slides and, after preparation with 20 per cent potassium hydroxide solution, were examined directly under the microscope for mycelia and spores. In addition, the scrapings were cultured on two mediums, one consisting of dextrose 4 per cent, peptone 1 per cent and agar 2 per cent, with a p_H adjusted to 5.8, and the other containing the aforementioned ingredients plus gentian violet in a final

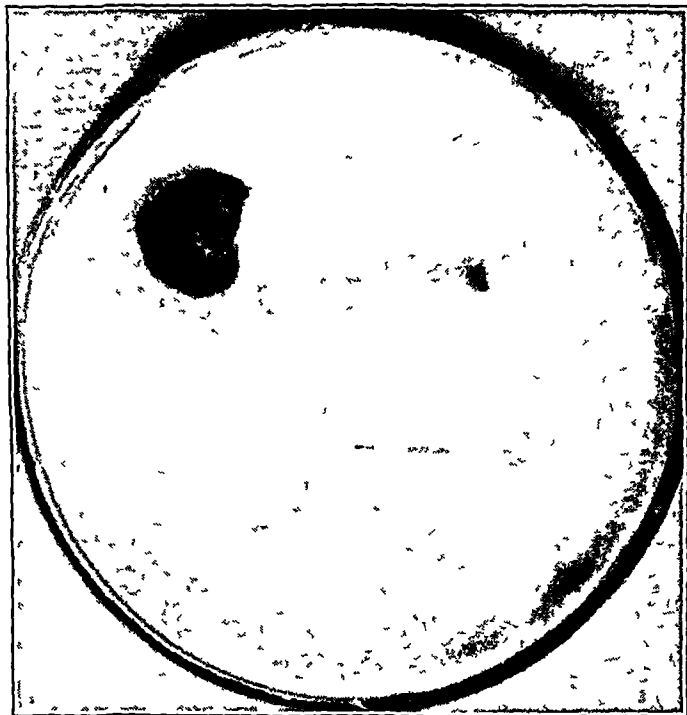


Fig 2—Control plate. The square centimeter of untreated leather insole can easily be seen, surrounded by a dense growth of *T. interdigitale*.

dilution of 1 to 500,000. As the cultures grew, transplants were made on plain Sabouraud mediums to differentiate the fungi. No culture was discarded as negative unless observed for a period of ten to fourteen weeks.

Of the 125 patients, 44, or 35 per cent, yielded mycelia on direct microscopic examination of the scrapings and, in addition, had positive cultures of fungi. In 39 cases the fungi were identified as *T. interdigitale*, in 2 as *T. rubrum*, in 2 as *T. rosaceum* and in 1 as *Monilia albicans*. The lesions of 20 patients, or 16 per cent, presented mycelia on direct microscopic examination of the scrapings, but the cultures were negative. Sixty-one patients, or 49 per cent, had negative results of both microscopic examination and culture.

TECHNIC

The method of application of the insole was simple. The patient was instructed to insert the treated insole into his shoes and to wear his socks and shoes in the regular manner. Each one continued his daily routine without interference. When the infection was extensive and the lesions extended on the dorsal surface of the foot, the insole was augmented with a rubber moccasin. This moccasin contained the same chemical ingredients as the insole and was worn over a pair of socks only at night. Only a few isolated patients required the use of these moccasins. In the control group of cases an untreated insole was substituted for the leather-chemical compound. In some instances the control period had to be short because of the rapid spread of the infection. The patients were examined at intervals of two weeks, and the clinical progress was noted. Records were kept as to the physical appearance of the lesions, such as scaling, fissuring, vesicle formation, degree of inflammation and denudation, as well as of the subjective symptoms, such as pruritus, perspiration and odor.

RESULTS

Percival⁸ and others have stated the belief that a diagnosis of fungous infection should not be made in the presence of clinical evidence of the disease unless the parasite has been demonstrated to exist in the lesion. Clinically I could not differentiate between those cases in which there were positive results of mycologic examination and those cases in which the results were negative. In order to avoid controversy I have grouped my cases in three divisions dependent on the mycologic findings, and I have tabulated the results accordingly.

The first group consisted of the 44 patients who presented positive cultures as well as positive microscopic findings. Twenty-seven of these were given the medicated insole therapy. In 19 the condition cleared clinically; the cultures became negative and mycelia could no longer be demonstrated on microscopic examination of scrapings at the original sites of infection. The period of therapy varied from one month to nine months, the average being four months. Eight patients were discharged during the period of treatment. All 8 showed definite clinical improvement, particularly in reference to subjective symptoms. It is interesting to note that at the time of discharge of these patients, 5 of them had negative cultures, though the mycelia could still be demonstrated on direct microscopic examination of the scrapings. Thirteen additional patients in this group were given a period of preliminary observation, during which time untreated insoles were inserted in their

8. Percival, G. H.: Fungus Infection of the Hands and Feet, Edinburgh M. J. 44:401-409 (June) 1937.

shoes This control period varied from one to five months, the average being two and one-fifth months No medication was employed during this period of preliminary observation, which resulted in either a spread of the infection or no clinical or mycologic improvement for all 13 patients Then treatment with the medicated insoles was instituted In 10 of these patients the condition cleared clinically as well as mycologically in from one to eight months, the average being three and one-half months Three patients were discharged during the course of treatment, and all 3 showed clinical improvement The 4 remaining patients in this group were discharged from the institution during the period of preliminary observation and before therapy could be instituted Thus, of 40 treated patients with positive cultures and positive microscopic findings, in 29, or 72.5 per cent, the condition was clinically and mycologically cleared, the average time approximating four months After the clearing, the patients were observed for a number of months for any recurrence of infection In 2 patients in this group either a relapse or a reinfection subsequently developed Comment on these 2 cases will be reserved for later discussion

The second group consisted of 20 patients who presented mycelia on direct examination of the scrapings of the lesions, the cultures of which were negative Eleven patients were given the medicated insole therapy In 8 of these patients the condition cleared clinically and microscopically in from one to three months, the average being two months Three patients were discharged during treatment, but all 3 showed decided clinical improvement Eight patients were given a period of preliminary observation as in the first group, varying from one to five months, with an average of three months During this period either there followed a spread of the infection or no clinical progress was noted Then medicated insole therapy was instituted In 7 of the 8 the condition cleared clinically as well as microscopically in one to six months, the average being two and one-half months One patient of this group was discharged from the institution before therapy could be started Thus, of 19 patients with negative cultures but positive microscopic findings, in 15, or 80 per cent, the condition was clinically and mycologically cleared in an average period of two and one-third months A subsequent observation period covering a number of months failed to reveal any evidence of recurrence of infection

The third division comprised that group of 61 patients with clinical evidence of dermatophytosis in whose cases cultures and microscopic findings were negative Thirty of this group were given medicated insole therapy, and the lesions cleared in from one month to five months, the average being two months For control, 31 patients were given untreated insoles and were observed for from one to three months, the average being two months During this control period the lesions

of 10 of the patients cleared spontaneously, the average time being one and one-half months. The remaining 21 patients serving as controls showed either a spread of the infection or no clinical improvement. Medicated insole therapy was then instituted, and in from one to seven months, with an average of two months, the infection cleared. Thus, of 51 treated patients with what clinically appeared to be dermatophytosis pedis, but without mycologic corroboration, in all 51, or 100 per cent, the condition was cleared in an average of two months. Most of the patients were subsequently followed for a number of months, but none of them showed evidence of recurrence of the infection.

Summary of Results of Treatment of Dermatophytosis Pedis with the Medicated Insoles

	Group 1	Group 2	Group 3
	Clinically Positive; Cultures Positive; Scrapings Microscopically Positive	Clinically Positive; Cultures Negative; Scrapings Microscopically Positive	Clinically Positive; Cultures Negative; Scrapings Microscopically Negative
Number of patients given preliminary observation	13	8	30
Average preliminary period, months.....	3.5	3	2
Number in which condition cleared or improved spontaneously	0	0	10
Number in which condition was unchanged or worse during preliminary observation....	13	8	20
Total number of patients treated.....	40	19	51
Number in which condition clinically and mycologically cleared	29	15	51
Average period for clearing, months.....	4	2.3	2
Number in which condition was clinically improved but not totally cleared.....	11	4	0
Number of patients failing to show improvement	0	0	0

The results of this survey are summarized in the accompanying table. The cases are grouped according to the mycologic and clinical findings.

REPORT OF CASES

CASE 1.—M. J., aged 15, had an eruption on both feet for a month, accompanied by scaling, fissuring, denudation of the cutis and erythema (fig. 3a). Pruritus, excessive perspiration and odor were present. Direct microscopic examination of the scrapings of the lesions yielded mycelia, and the cultures were positive for *Monilia albicans*. Medicated insole therapy was then instituted. In two months the subjective symptoms disappeared, and in four months the lesions cleared clinically (fig. 3b). Fungi could no longer be demonstrated in the scrapings of the original sites either by direct microscopic examination or by culture. The skin remained clinically and mycologically clear for the following eight months.

CASE 2.—L. L., aged 15, had had an eruption between the toes and on the dorsal surface of both feet for the past six months. The lesions were characterized

by scaling, fissuring formation, denudation of the cutis and erythema (fig 4a). Direct microscopic examination of the scrapings of the lesion yielded mycelia, and the culture was positive for *T. phyton rubrum*. Because of the extensive involvement of the dorsal surfaces of both feet, the medicated insole therapy was augmented with rubber moccasins containing the same chemical ingredients as the insoles. In three months the eruption cleared (fig 4b), and the results of direct microscopic examination of the scrapings at the original sites as well as the cultures became negative.

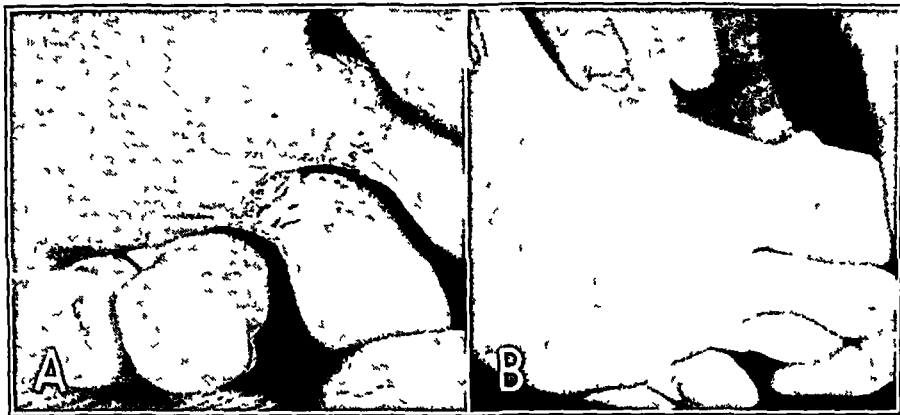


Fig 3 (case 1)—*A*, cultures positive for *M. albicans*. Note the clinical appearance of the lesions before treatment. *B*, after four months of therapy. Cultures and direct microscopic examinations now negative.



Fig 4 (case 2)—*A*, the lesions before treatment. Cultures positive for *T. rubrum*. *B*, after three months of therapy. Cultures and direct microscopic examinations now negative.

CASE 3—J. L., aged 17, had an eruption on both feet, consisting of scaling, fissuring, vesicle formation and erythema (fig 5a). Pruritus, profuse perspiration and a strong odor accompanied the eruption. Mycelia could be demonstrated on direct microscopic examinations of the scrapings of the lesions, but repeated cultures were negative. A control period of four months was instituted, but no improvement was demonstrable at the end of that time. Because of the extensive involvement of the dorsal surfaces of both feet the medicated insole therapy was augmented with medicated rubber moccasins worn at night. In four months the

lesions disappeared (fig. 5 *b*), and mycelia were no longer demonstrable on direct microscopic examination of the scraping of the original sites.

COMMENT

Although this survey was limited to 125 patients, many interesting observations were recorded. It was noted that the younger the patient and the more recent the infection, the more quickly amenable was the infection to treatment. None of the patients wearing the medicated insoles complained of any discomfort during the period of therapy. However, 2 patients did experience a slightly tingling or burning sensation with the wearing of the medicated rubber moccasins.

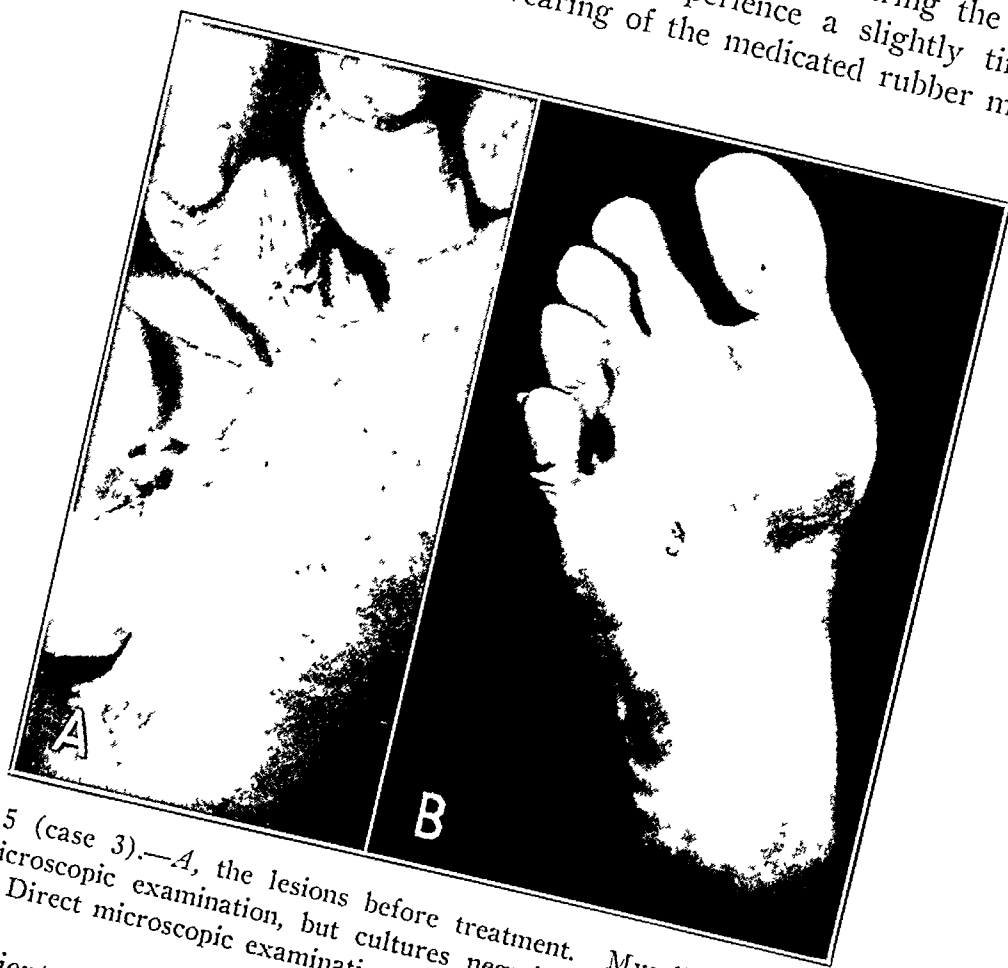


Fig. 5 (case 3).—*A*, the lesions before treatment. Mycelia demonstrable on direct microscopic examination, but cultures negative. *B*, after four months of therapy. Direct microscopic examination and culture gave negative results.

Two patients had either a relapse or a reinfection. Both patients originally had had positive cultures and, after clearing, negative results of clinical and mycologic examinations for three months. With the relapse or reinfection mycelia could be demonstrated on microscopic examination of the scrapings of the new lesions, but repeated cultures remained negative. In both patients the condition eventually cleared again. During this study only 7 new cases appeared in the institution after the initial survey of all the inmates. In 6 of these cases fungi were shown by microscopic examination of scrapings. This is a surprisingly

low number for approximately a year. This observation suggests the possibility of the general employment of these medicated insoles as a prophylactic measure against dermatophytosis pedis.

SUMMARY

A new and simple method of treatment for dermatophytosis pedis is described.

The fungistatic action of leather insoles containing rubber impregnated with 8-hydroxyquinoline, parachlorometaxylenol and chlorothymol against *T. interdigitale* is demonstrated.

Of 40 treated patients with positive cultures and mycelia demonstrable on direct microscopic examination, in 29, or 72.5 per cent, the condition was clinically and mycologically cleared in an average period of four months.

Of 19 treated patients with negative cultures but with mycelia demonstrable on direct microscopic examination, in 15, or 80 per cent, the condition was clinically and mycologically cleared in an average period of two and one-third months.

Of 51 treated patients with negative cultures and no microscopic findings, in 51, or 100 per cent, the condition was cleared in an average period of two months.

Dr. Samuel S. Epstein participated in the mycologic investigations.

1245 Union Street

GENERALIZED HERPES ZOSTER ASSOCIATED WITH LEUKEMIA

UDO J. WILE, M.D.

Professor of Dermatology and Syphilology

AND

HERBERT H. HOLMAN, M.D.

Instructor in Dermatology and Syphilology
ANN ARBOR, MICH.

The occurrence of generalized herpes zoster in association with leukemia was first reported by Fischl in 1914. A review of the literature has disclosed 32 cases of this syndrome. The following tabulation presents the salient features of the individual cases.

Author	Sex	Age	Type of Leukemia
Fischl, F.: Arch. f. Dermat. u. Syph. 118 : 553, 1913-1914....	Male	61	Lymphatic
Weber, F. P.: Brit. J. Dermat. 28 : 13, 1916.....	Male	59	Lymphatic
Proebsting: Deutsche med. Wehnschr. 47 : 116, 1921.....	?	?	Lymphatic
Lepp, F.: Zentralbl. f. Haut- u. Geschlechtskr. 19 : 870, 1926	Female	59	Leukemic lymphadenosis
Ziel, R.: Med. Klin. 22 : 985, 1926.....	Male	67	Lymphatic
Jadassohn, J.: Zentralbl. f. Haut- u. Geschlechtskr. 20 : 23, 1926	Male	68	Not specified
Kreibich, E.: Zentralbl. f. Haut- u. Geschlechtskr. 23 : 612, 1927	Male	70	Lymphatic
Zeisler: Arch. Dermat. & Syph. 17 : 140 (Jan.) 1928.....	?	?	Lymphatic
Freund, H.: Arch. f. Dermat. u. Syph. 154-155 : 476, 1928	Female	57	Not specified
Münsterer, H.: Dermat. Wehnschr. 87 : 121, 1928.....	Male	45	Lymphatic
Glaubersohn, S.: Dermat. Wehnschr. 87 : 1422, 1928.....	Female	52	Lymphatic (leukemic)
Keining, E.: Dermat. Wehnschr. 86 : 665, 1928.....	Male	58	Lymphatic
Marigondas: Gazz. d. osp. 49 : 549, 1928.....	Male	72	Lymphatic (?)
Halle, H.: Arch. f. Dermat. u. Syph. 159 : 238, 1930.....	Male	68	Myeloid (?)
Gotttron and Jakob: Zentralbl. f. Haut- u. Geschlechtskr. 32 : 548, 1930	Male	63	Lymphatic
Dostrowsky, A.: Dermat. Wehnschr. 92 : 685, 1931.....	Male	55	Lymphatic
Katz, F.: Arch. f. Dermat. u. Syph. 96 : 725, 1933.....	Female	49	Lymphatic
Arzt, L.: Dermat. Wehnschr. 96 : 561, 1931.....	Female	63	Lymphatic
Markus, cited by Marques, J. F.: Arch. f. Dermat. u. Syph. 176-177 : 295, 1938	Male	72	Lymphatic
Markus, cited by Marques, J. F.: Arch. f. Dermat. u. Syph. 176-177 : 295, 1938	Male	55	Lymphatic (aleukemic)
Wolfram and Marques, cited by Marques, J. F.: Arch. f. Dermat. u. Syph. 176-177 : 295, 1938.....	Male	70	Lymphatic
Buschke: Zentralbl. f. Haut- u. Geschlechtskr. 39-40 : 496, 1932	Male	55	Lymphatic
Haack, K.: Dermat. Wehnschr. 95 : 1819, 1932.....	Male	55	Lymphatic
Proppe, A.: Dermat. Ztschr. 69 : 39, 1934.....	Female	67	Lymphatic
Brandt: Acta dermat.-venereol. 14 : 514, 1934.....	?	?	Lymphatic
Brandt: Acta dermat.-venereol. 14 : 514, 1934.....	Male	72	Lymphatic
Skerr, J.: Arch. Dermat. & Syph. 34 : 809 (Nov.) 1936....	Male	50	Lymphatic (aleukemic)
Skeer, J.: Arch. Dermat. & Syph. 34 : 809 (Nov.) 1936....	Female	40	Lymphatic
Lynch, F. W.: Arch. Dermat. & Syph. 34 : 775 (Nov.) 1936....	Male	53	Lymphatic
Damm, cited by Barney, R. E.: Arch. Dermat. & Syph. 37 : 238 (Feb.) 1938.....	Male	48	Lymphatic
Marques, J. F.: Arch. f. Dermat. u. Syph. 176-177 : 295, 1938	?	?	Not specified
Baneroff, I. R., and McEachern, K. L.: Personal communication to the author.....	Male	76	Lymphatic
	Female	63	Lymphatic

From the University of Michigan Medical School, service of Dr. Udo J. Wile.

Lymphatic leukemia was by far the most common type of leukemia noted, being present in 27 (93 per cent) of the 29 cases in which the type of leukemia was reported. An aleukemic type of lymphatic leukemia was present in 3 (11 per cent) of the 27 cases. A case of probable myeloid leukemia and a case of leukemic lymphadenosis were observed. The type of leukemia was not specified in 3 cases (9 per cent). The average age of the patients reported was 60. Men were affected in



Fig 1 (case 1)—Unilateral grouped vesicular eruption on the left upper extremity

20 cases (71.4 per cent), whereas women were affected in only 8 cases (28.6 per cent).

During the past two years 2 cases of generalized herpes zoster in association with lymphatic leukemia were observed in the department of dermatology and syphilology of the University of Michigan Hospital.

REPORT OF CASES

CASE 1—A. J. B., a married man aged 58, was first examined in the Department of Dermatology and Syphilology of the University of Michigan Hospital on Aug 10, 1938. His chief complaints were "skin eruption and leukemia." He had been

well up to two years prior to admission, at which time he first noticed swelling in the neck, axillas and inguinal regions. The diagnosis of leukemia was made at that time from an examination of the blood. Before admission to this hospital he had received roentgen therapy of high voltage on eight occasions, after which the enlargement of the lymph glands diminished. He first noted the appearance of an eruption on his face four weeks prior to admission. During the ten days immediately preceding admission, lesions associated with severe pain developed on the left hand and forearm and became progressively worse. Seven days after the onset a generalized eruption developed.

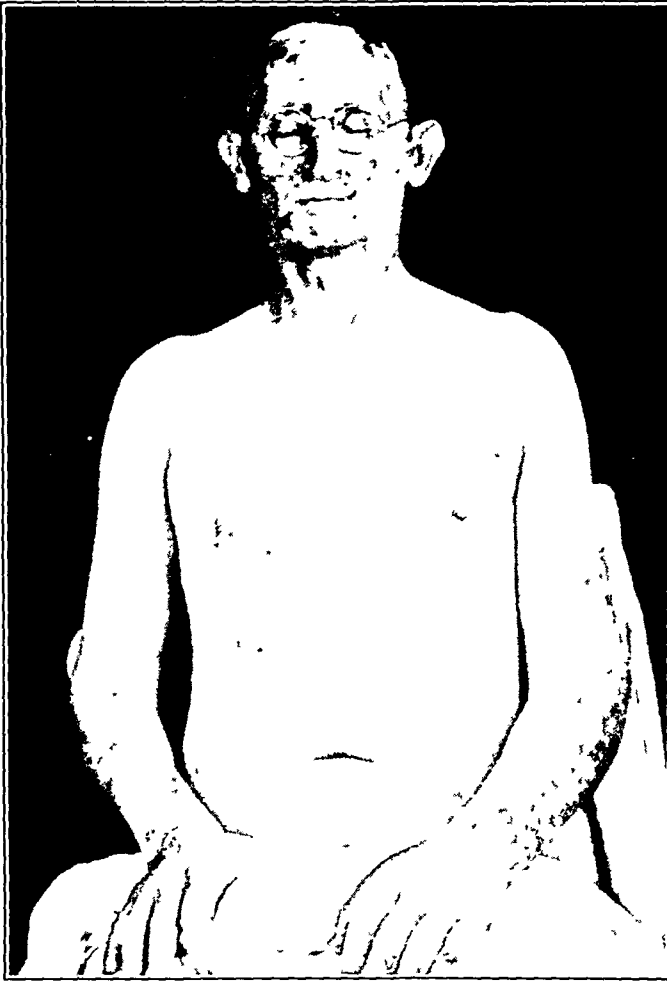


Fig. 2 (case 1).—Generalized vesicular eruption.

The past and family histories had no apparent bearing on the case.

Initial examination revealed a rather well developed white man with marked dyspnea. His temperature was 99.2 F., pulse rate 100 and respiratory rate 24. The skin showed a generalized eruption, involving chiefly the left upper extremity, which also was extremely edematous and could not be moved actively by the patient. There was a strikingly grouped, vesicular and bullous eruption extending from the midportion of the arm, largely on the extensor surface, over the forearm and onto the fingers, which were extremely edematous and tender. The groups of vesicles were superimposed on a deeply erythematous, papular, infiltrated base. Severe secondary infection was present in the vesicular lesions (fig. 1). The face presented small papules and nodules, which were distinctly infiltrated. Some of these nodules

disclosed superimposed vesicles, while others presented excoriated surfaces. The eruptions on the trunk and on right arm were of similar appearance, characterized by small vesicles superimposed on a brightly erythematous base. The lesions on the right side of the body revealed little or no infiltration (fig 2).

Enlarged lymph glands were found in the inguinal, axillary and cervical regions. The skin overlying these areas showed telangiectasia and pigmentation, apparently due to previous roentgen therapy to these sites. The liver and spleen were palpably enlarged. The heart and lungs were normal.

Initial study of the blood at the Simpson Memorial Institute for Blood Diseases showed 80 per cent hemoglobin (12.4 Gm per hundred cubic centimeters) by the Sahli method, 4,180,000 red blood cells and 36,800 white blood cells per cubic millimeter. A differential smear showed 15 per cent polymorphonuclear neutrophils, 66 per cent large lymphocytes, 18 per cent small lymphocytes and 1 per cent mono-



Fig 3 (case 2) —Unilateral grouped vesicular eruption on the scalp

cytes. The lymphocytes were atypical and immature. A diagnosis of chronic lymphatic leukemia was made. The result of a Kahn test for syphilis was negative. The urine was normal. A biopsy was performed, and histologic examination revealed increased cornification with underlying vesiculation. No lymphoblastomatous infiltrations were noted.

The patient was hospitalized, and the left arm was treated with dressings soaked in hot solution of magnesium sulfate, with much improvement. The left forearm and hand were splinted to prevent wrist drop and contracture of the fingers. One transfusion of 500 cc of citrated blood was given. The limitation of motion of the left upper extremity was interpreted by members of the department of neurosurgery as being secondary to leukemic infiltration of the cervical roots of the spinal cord.

High voltage roentgen therapy to the cervical spine was productive of definite symptomatic relief as well as of gradual return of function of the left wrist (but not of the fingers). The cutaneous manifestations showed definite but slow improve-

ment during the course of hospitalization. The patient received periodic high voltage roentgen therapy to the lymph glands, spleen and liver, with subsequent decrease in the total white blood cell count to 28,000 per cubic millimeter.

The patient was discharged from the hospital on October 20. He returned to the dermatologic outpatient clinic on November 18, complaining of shooting pains in the left arm. Study of the blood at this time revealed 72 per cent hemoglobin (11.4 Gm. per hundred cubic centimeters), 4,260,000 red blood cells and 24,100 polymorphonuclear neutrophils, 2 per cent eosinophils, 12 per cent small lymphocytes, 1 per cent large lymphocytes and 53 per cent atypical cells, including monocytes and other cells of probable endothelial origin. The patient last visited the hospital on



Fig 4 (case 2).—Isolated vesicles and blebs on the upper extremities and trunk.

Jan. 4, 1939, at which time bluish, nummular, infiltrated lesions were noted on the face. These were thought to be leukemids, but, unfortunately, biopsy material could not be obtained for microscopic confirmation. Almost normal function had returned to the left elbow and to the wrist joints. Active motion in the finger joints remained impaired.

It was later learned that the patient died of pneumonia in January 1940 outside of the hospital. Permission for autopsy could not be obtained.

CASE 2—F. G., a white factory worker, aged 52, had been examined at the Henry Ford Hospital, Detroit, prior to admission to the University of Michigan Hospital. At that time the diagnosis of chronic lymphatic leukemia was established by study of the blood and histologic examination of an axillary lymph node. The vesicular lesions present at that examination were thought to be associated with the

leukemic state, but the zosteriform configuration was lacking. Moderate improvement followed high voltage roentgen therapy.

The patient was admitted to the dermatologic service of the University of Michigan Hospital on Sept. 30, 1939, with the chief complaint of "skin trouble." He had been well until fifteen months prior to admission, at which time he first complained of weakness and ease of fatigue. The eruption was first noted at this time and persisted until the time of admission. He had lost 35 pounds (16 kg.).

Examination revealed that he was fairly well nourished, well developed and apparently chronically ill. The skin presented an eruption which consisted of two distinct types of lesions and which was sparsely generalized, involving predominantly the head and the upper extremities. The right frontoparietal region of the scalp presented closely approximated, grouped, thick-walled vesicles, some of which had already become confluent to form blebs, and all of which were superimposed on brightly erythematous bases. This eruption was strikingly delimited by the midline of the scalp. There was a ruptured bleb to the left of the midline on the forehead. The left eye was swollen almost completely shut (fig. 3). The left upper extremity was severely involved by a brawny induration, superimposed on which were numerous groups of thick-walled vesicles and bullae in a roughly linear band, extending downward over the anteromedial aspect of the arm and the upper part of the forearm. There was some limitation of active motion of the left arm. The dorsa of both hands and forearms presented bluish red, coin-sized, firm nodules, with thick-walled blebs superimposed on them (fig. 4). The remainder of the eruption was composed of bluish red, split pea-sized to coin-sized, infiltrated nodules scattered over the trunk and lower extremities.

Soft, tender lymph nodes, varying in size from that of a pigeon's egg to that of a hen's egg, were present in the cervical, axillary and inguinal regions. The spleen was palpable a fingerbreadth below the left costal margin, and the liver was palpable 2 fingerbreadths below the right costal margin. The heart and lungs were normal.

A blood count revealed 95 per cent hemoglobin and 128,000 white blood cells per cubic millimeter. A differential smear showed 92 per cent lymphocytes, 7 per cent polymorphonuclear neutrophils and 1 per cent monocytes. The result of a Kahn test for syphilis was negative.

The family of the patient was not cooperative in respect to further study, having been informed previously of the hopelessness of the patient's condition. Consequently, further data are not available, nor has the patient been heard from since the initial examination.

SUMMARY

Two cases of generalized herpes zoster in association with lymphatic leukemia are reported.

A review of previously reported cases is presented.

Generalized herpes zoster when complicating the leukemic state occurs most frequently in middle-aged men afflicted with lymphatic leukemia.

ACNE VULGARIS

REVIEW OF HISTOLOGIC CHANGES OBSERVED IN EARLY LESIONS

FRANCIS W. LYNCH, M.D.

ST. PAUL

The study of acne is important both because of the frequent occurrence of the disease and because the results of treatment are relatively unsatisfactory. There seems no end to the number and variety of therapeutic agents suggested for use in cases of acne. While many of the suggestions have been well considered and the results of their application well controlled and tested before being reported to the members of the medical profession, their very number and variety suggest that investigative energy might better be devoted to the unsolved fundamental problems of this disease. Among these problems are the relation of acne to the seborrheic state, to infection, to puberty, to the endocrine system and to the metabolism of carbohydrates and fats.

Further work on the association between acne and seborrhea is dependent on more accurate knowledge of the latter condition, particularly the change in the nature and amount of sebum, as well as on confirmation and extension of the more recent studies on the bacteriology of seborrhea.

There can be no denial of a relation between acne and the endocrine system, but there is no satisfactory evidence that the eruption is directly dependent on the demonstrated deficiencies of male or female hormones. After more numerous and more detailed chemical analyses have been made, the experimental approach must be used before conclusions can be drawn.

It is evident that there is some connection between acne and the diet, but this relation is frequently overemphasized. Weighed dietary regulation, chemical studies of the blood and tissues and prolonged clinical observation might clarify such a relation. The association with carbohydrate metabolism is less important, or at least less obvious, than was formerly thought, but interest in lipid metabolism has been reawakened recently by the therapeutic claims of Sutton.

Since the histologic and bacteriologic investigations of acne were among the first extensive dermatologic studies, it may seem presumptu-

Read at the Sixty-Third Annual Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., May 30, 1940.

From the University of Minnesota, Division of Dermatology, Dr. H. E. Michelson, Director, and the Students' Health Service, Dr. Ruth Boynton, Director.

ous to add to the existing descriptions. However, a critical review suggests that many of the subsequent histologic descriptions are based on rather limited original observations and more on acceptance of Unna's excellent treatise on the subject.¹

In spite of the need for solution of the problems previously mentioned, it may be worth while to review the pathologic changes of acne, because of the relative paucity of records of direct observations and because descriptions of the early lesions of this disease are often brief



Fig 1 ($\times 64$)—Early lesion of acne, showing a follicular plug made up of hyperkeratotic scale and retained sebum. There is only a moderate degree of perivascular lymphocytic infiltration.

and vague. The inflammatory papules and pustules have been more frequently described, and the observations concerning these lesions fit the modern concepts of cutaneous infection so well that they can probably be accepted.² Newer histologic technic might be hoped to allow addition to or reinterpretation of the older descriptions by Unna.

1 Unna, P. G. *The Histopathology of Diseases of the Skin*, translated by N. Walker, New York, Macmillan & Company, 1896, pp. 352-361.

2 Whitfield, A. *Seborrhea and Its Consequences*, *Internat. Clin.* 2: 183, 1910.

The sections reviewed in this study were made from early lesions of 30 patients with acne. They were usually removed from the back but in several instances were taken from the face. Several normal follicles were studied for comparison, as were some larger papules and pustules of acne. In addition to the use of hemotoxylin and eosin, sections were stained to show elastic tissue, lipoids and bacteria.

The clinical description of the lesion as a normal follicle, a comedo or a papule was not always supported by the microscopic observations, and it became evident that the age and stage of a comedo cannot be

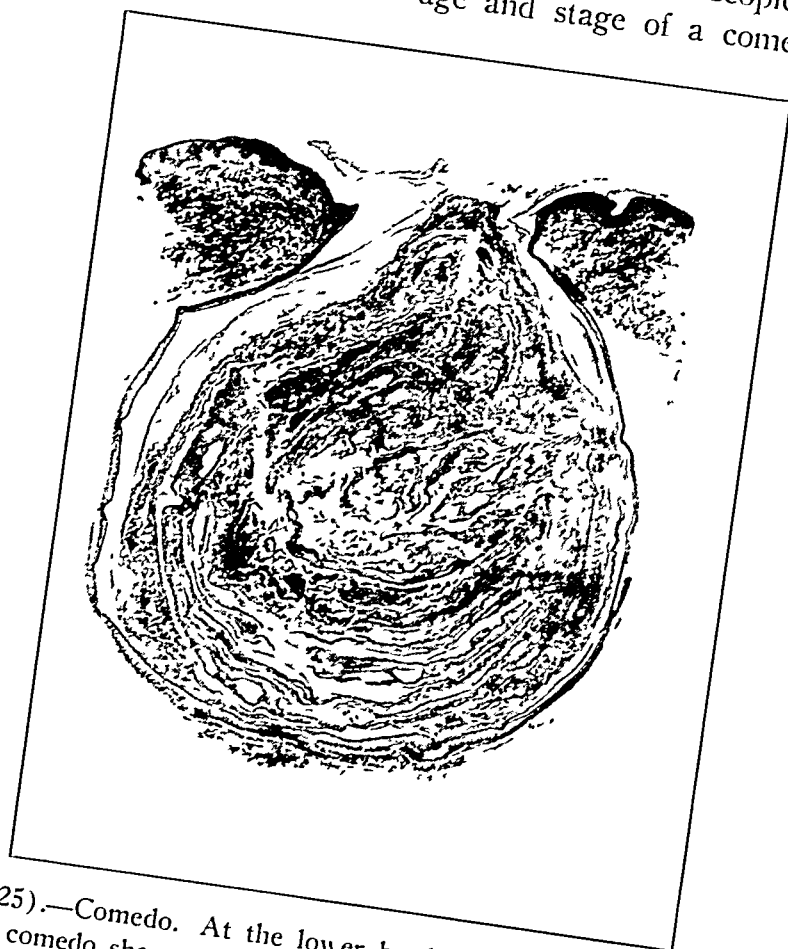


Fig. 2 ($\times 25$).—Comedo. At the lower border is a remnant of the hair shaft and bulb. The comedo shows the "onion peel" lamellar arrangement characteristic of older lesions.

judged by its gross appearance. There was further confusion because one section of a follicle may show only slight perivascular infiltration while other sections of the same follicle show a mass of infiltrate situated only at one side of the follicle rather than encircling it.

Since it is impossible to determine when a comedo is about to form, this study was begun with examination of follicles from the seborrheic areas of the backs of patients with acne. In a few sections normal anatomic conditions prevailed, but in others there were more than normal perivascular lymphocytic infiltration and some vasodilatation and con-

gestion In another, the pathologic changes were unexpected, and it is likely that the tissue represented a small papule undergoing involution There was a mass of infiltrate enclosing what appeared to be atrophic sebaceous gland tissue

Several follicles thought clinically to contain comedos showed only the same changes observed in the more nearly normal follicles A large comedo showed no inflammatory reaction in the adjacent tissues In 1



Fig 3 ($\times 150$) —Epithelial atrophy at the mouth of the follicle The Weigert stain also shows an absence of the finer elastic fibrils near the epithelial wall surrounding this comedo

case there was a parakeratotic plug in the follicle, with perifollicular as well as perivascular infiltrate At one side of another comedo a small inflammatory infiltrate was observed In a few instances more advanced changes were noted In 1 of these there were epithelial atrophy within the follicular mouth and loss of the fine elastic tissue immediately surrounding the follicle Very little infiltrate was present In another case giant cells were seen in the infiltrate around a comedo, and there was

evidence of atrophy of the sebaceous glands. One of the larger comedos consisted chiefly of a lamellated, hyperkeratotic scale with some areas of parakeratosis. The remnant of the hair bulb was very small. In the upper layers of the cutis only perivascular lymphocytic infiltrate was present, but deeper, around the base of the follicle, the changes were much more pronounced. There was moderately intensive infiltration with large and small lymphocytes, with occasional plasma cells and a few

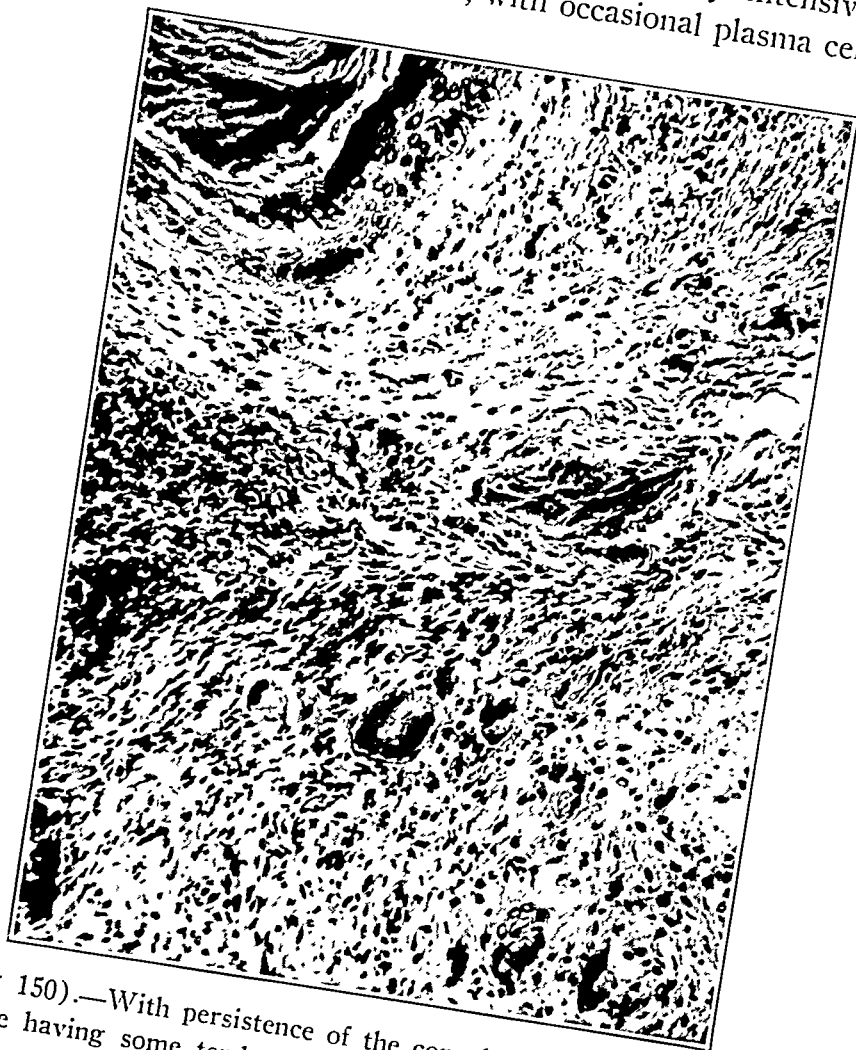


Fig. 4 ($\times 150$).—With persistence of the comedo there is a polymorphous cellular infiltrate having some tendency to organization, and there are a few giant cells.

giant cells. There were many fibroblasts with numerous small fibrils. Elastic tissue was absent throughout the infiltrated areas.

In several lesions which were clinically regarded as small papules only follicular plugging and slight perivascular infiltration were observed. In others there was an inflammatory mass adjacent to a follicle, apparently representing an inflammatory reaction around fragmented epithelial structures. The infiltrate resembled that previously mentioned, but a moderate number of polymorphonuclear leukocytes were present in these

areas, in contrast to sections of earlier lesions. Immediately superior to this small inflammatory mass but in the surface epithelium or perhaps within the follicle was a very small abscess with some polymorphonuclear leukocytes.

In most sections taken at early stages the elastic tissue was undisturbed though the finer fibrils were absent around older lesions. In areas of inflammatory infiltration elastic tissue could not be demonstrated, though fibroblastic activity was often evident.

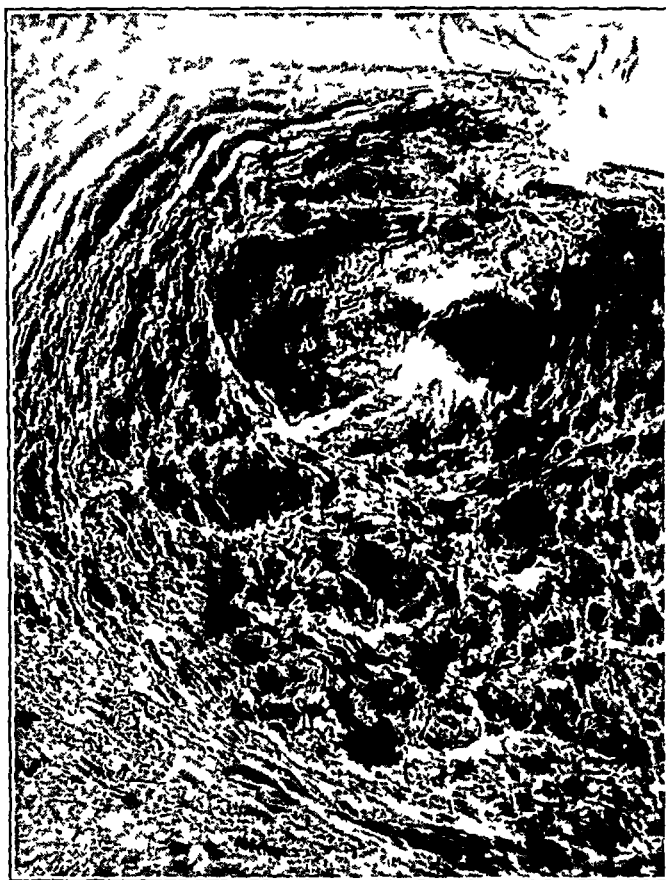


Fig 5 ($\times 300$)—Lymphocytic infiltration and fibroblastic reaction have developed around irregular pieces of tissue, which are stained with sudan III

Lipoid stains in most of the sections showed no abnormal change except the presence of the sebum in the follicular plug. There was no evidence of extrusion of lipid into the tissues through the follicular wall. In lesions containing masses of infiltrate the special stain usually showed some fat within the mass, but the usual tissue stains suggested that this fat was present in epithelial cells which were probably part of a former sebaceous gland.

In spite of numerous and extensive studies there remains considerable confusion as to the bacteriology of seborrhea and acne, due partly to the variety of descriptive terms used by the observers and partly to the pleomorphism of several of the organisms concerned. Since *Pityrosporum ovale*, *Corynebacterium acnes* and several staphylococci are found frequently on normal as well as on seborrheic skin, it is difficult to determine whether any of them is pathogenic. The belief that the acne bacillus is pathogenic was once vigorously supported by most inves-



Fig. 6 ($\times 250$).—At the left of the follicle, near its mouth, there is a small abscess showing necrosis and polymorphonuclear leukocytes, though the lesion was still clinically regarded as a papule.

tigators, but there is now considerable doubt. There is doubt also whether the cocci are secondary invaders or perhaps saprophytes or (less probably) the etiologic organisms of acne.

I am unprepared to enter into any bacteriologic discussion, and I can only hope that the record of my observations will not further confuse. In the identification of the organisms in the sections of tissue, I was greatly aided by a bacteriologist who carried out cultural studies on these and

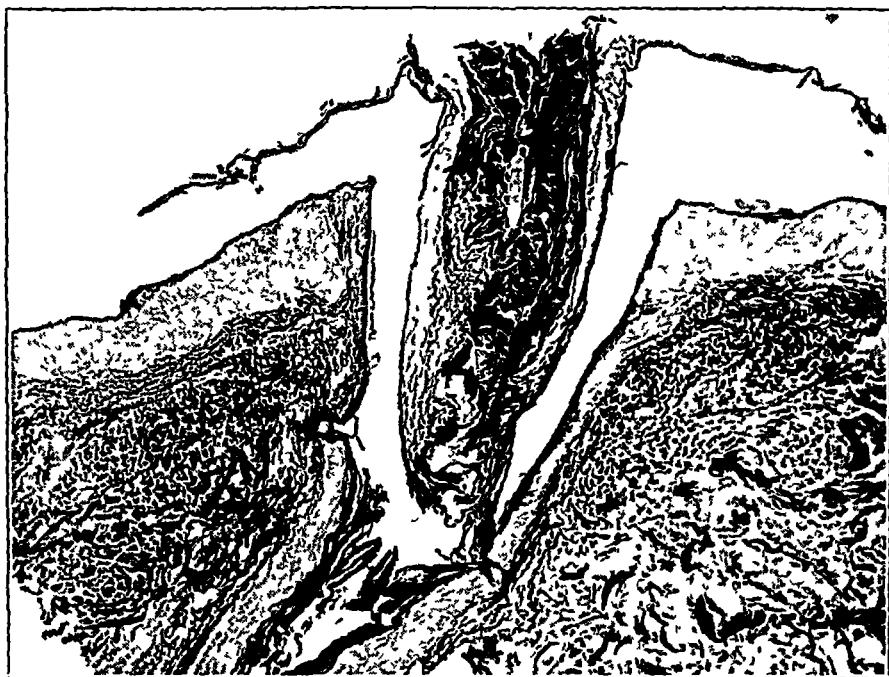


Fig 7 ($\times 75$) —Within the comedo are darkly stained masses of diphtheroid bacilli, particularly evident near the lanugo



Fig 8 ($\times 1,800$) —The pleomorphism of the diphtheroid bacilli is evident in these organisms from the mouth of a follicle containing a comedo. These organisms are much smaller than the so-called bottle bacillus

other patients.³ Cultures of material from the skin of normal persons and of persons with acne showed the fairly constant presence of two organisms apparently identical with those observed in the sections of tissue. A gram-positive coccus was identified as a white staphylococcus. The gram-positive bacillus was a microaerophilic organism presenting a variable appearance: large coccoid forms, diphtheroid rods, fine rods, beaded forms, "seed" forms and a "plasma cell" form. The rods were occasionally paired or in short chains. Though decided pleomorphism of the bacilli was noted in a given culture, a single morphologic type usually predominated. The "plasma cell" forms described by Ketron (acne B)

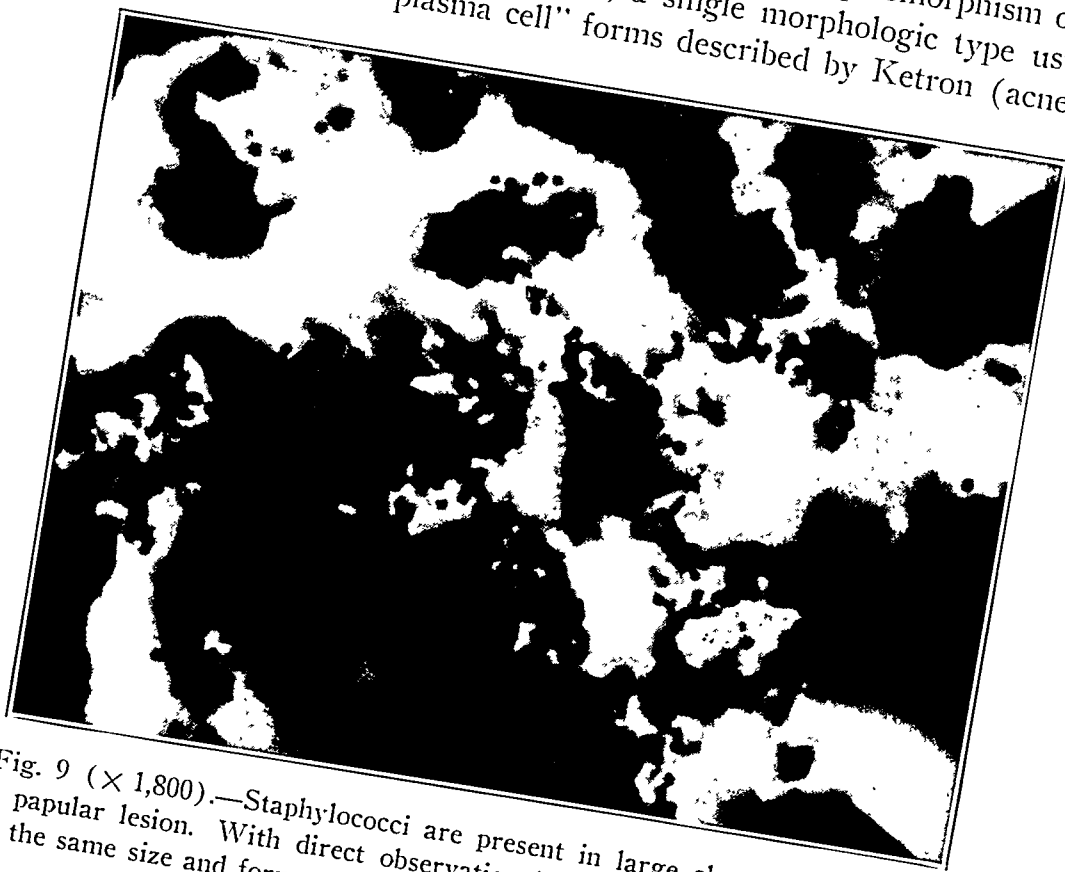


Fig. 9 ($\times 1,800$).—Staphylococci are present in large clumps within a follicle of a papular lesion. With direct observation it is evident that the organisms all have the same size and form.

remained more consistent in their differentiation from the other types than did the other forms. In smears from the lesions phagocytosis was observed only occasionally and was practically limited to diphtheroid organisms.

The same organisms were seen in many of my histologic preparations. Diphtheroid bacilli were observed in nearly all sections of simple follicles and comedos; they were usually most numerous at the follicular orifice and along the lanugo. These organisms were usually seen in

3. Help and advice were given by Dr. A. T. Henrici, professor, and Miss Margaret Nickle, graduate student, of the Department of Bacteriology, University of Minnesota.

large clumps, but the clumps were scattered through the follicular contents without much regularity. The diphtheroid bacilli showed pleomorphism: some were coccoid forms, others were rather fine rods and others, because of the light staining central band and the darker rounded ends, resembled diplococci. In some instances the short rods were paired and a few were in chains. Staphylococci were seen in none of the normal follicles but were present in several of the comedos and papules, twice in considerable numbers; in these lesions few or no diphtheroid organisms were seen. *Pityosporum ovale* was present in many of the sections.

The presence of bacteria was almost entirely limited to the contents of the follicle. In only 1 instance were a few bacilli noted in the epithelial wall of the follicle and in the surrounding connective tissues. In the absence of any inflammatory reaction around these organisms one could not be sure whether they might not have been introduced into the tissues accidentally during cutting of the sections.

SUMMARY

Examination of a series of 30 early lesions of acne affords no clue as to the cause of the comedo. The sebaceous skin of persons with acne presents varying degrees of perivascular infiltration and some follicular plugging with sebum and hyperkeratotic scale. The clinical comedo may present little more than these changes, though characteristically the plug is larger and appears to be more firm and parakeratosis is evident. The inflammatory reaction, aside from slight degrees of perivascular infiltration, appears first around glandular epithelial fragments. Perhaps the persistence of a comedo leads to atrophy and fragmentation of some of the glandular appendages of the follicle. These fragments then become surrounded with an infiltrate of large and small lymphocytes, some plasma cells and even giant cells. Polymorphonuclear leukocytes do not appear until later. The connective tissue cells proliferate, and this eventually results in a basket of fibers around the base of the follicle.

Special stains of sections from early lesions show the bacteria confined to the follicular contents and not invading the wall of the follicle, its glandular appendages or the adjacent tissues. If it could be assumed that bacteria pass from the comedo through the follicular wall into the connective tissues, the inflammatory reaction which develops in the tissues could be easily understood. Although this possibility exists, it was not possible to demonstrate bacteria in the early inflammatory infiltrate, and one must search elsewhere for the immediate cause of this inflammation. Bacterial toxins may be suspected, and there is the possibility that there may have been a few bacteria in the tubule or gland around which the reaction developed, but such organisms were not seen.

Whereas a comedo containing no demonstrable bacteria may be associated with at least a slight degree of inflammatory reaction, it is possible to find larger comedos with a great number of organisms but no surrounding inflammation. Such observations leave doubt as to the significance of the bacteria. There remains the possibility that the organisms are saprophytes or secondary invaders. A possible synergistic action is unlikely, because in large numbers is seldom observed in a single lesion. Since only the early lesions of acne are under consideration, the question of secondary bacterial invasion is not of immediate concern.

Although this study gives little evidence of a bacterial causation of acne, additional information should be obtained by continued bacteriologic, serologic and immunologic experimentation. Chemical studies may also be of aid in determining whether the inflammatory nature of the acne lesion can result from bacterial production of butyric acid in the follicle.

The nature of the cellular reaction of the acne papule has suggested to some observers that it develops around lipoids extruded from the follicle. In this series of sections there was no evidence of follicular rupture or of free fat in the tissues. Observations on these tissues suggested that the inflammatory reaction developed around atrophic glandular structures (having a lipid content demonstrable with special stains) rather than around free globules of fat. The fats within the inflammatory mass appeared to be present in sebaceous gland cells rather than in histiocytes. These studies do not allow any conclusions as to a possible relation between acne and the general metabolism of lipoids.

Thus it is my conclusion that the inflammatory phase of the acne papule can arise without apparent rupture of the follicle and without demonstrable bacterial invasion of the follicle wall, the glands or the connective tissues. The papule frequently develops as an inflammatory reaction around remnants of atrophic sebaceous glands which are perhaps a sequel to the stasis and pressure caused by the comedo within the follicle. The nature of the mechanism of production of the comedo remains obscure, as does the part played by the bacteria throughout the development of the lesion.

ABSTRACT OF DISCUSSION

DR. MARION B. SULZBERGER, New York: Dr. Lynch has done a fine, objective piece of work. This presentation is a distinct contribution. One can never tell how much one may be able to build in the future on the established foundation of factual, objective observations of this kind. The subject of the pathogenesis of acne vulgaris is one of the most important with which dermatologists have to deal. I should like to ask Dr. Lynch whether he had the opportunity to examine bacteriologically lesions from various parts of the body. I think that what he has said has forged another link in the chain of proof that micro-organisms, or

at least micro-organisms which are known and demonstrable at present, are probably not of etiologic significance in the production of acne vulgaris. I wonder whether Dr. Lynch was able to substantiate a claim that the facial lesions of acne vulgaris abound with bacteria, bottle bacilli, pityrospora, staphylococci, both white and yellow, and other micro-organisms, but that when one examines apparently identical lesions on the covered parts of the back and chest one will often find them sterile or almost sterile. This would be additional evidence that the micro-organisms demonstrated in the facial lesions are probably not of basic etiologic significance in acne vulgaris.

To return to the second observation, I think, if I interpreted Dr. Lynch correctly, that his idea of the pathogenesis of acne is not very dissimilar from that which has been held previously and which was discussed at length in a study by Drs. Rostenberg and Sher and me several years ago. We stated that the primary lesion is the plugging of the follicle, which leads to the comedo, and that only secondarily, for some reason not definitely known, does inflammation develop around some of the plugged follicles.

There are several possible explanations.

One is that the follicle acts as a foreign body and that the inflammation is a foreign body reaction to the follicle itself. That, apparently, is not the case, according to Dr. Lynch's observations.

The second possibility is that material from the plugged follicle transudes or passes through the epithelium and into the cutis around the follicle, that lipoids or substances derived from micro-organisms or other material thus infiltrate the cutis, and that the inflammatory reaction is a response to this infiltrating foreign material. Apparently, according to Dr. Lynch's studies, this hypothesis also does not apply. It would not explain the localization of the infiltrate which he has demonstrated.

The third possibility is that the atrophy and disintegration of the follicle wall, which are due to pressure of the plug, lead to manufacture of products which act as foreign bodies (lipoids and perhaps other products) and that the inflammation is a reaction to that disintegrating material of the wall itself and not to material coming from within the follicular orifice. The localization of the earliest visible infiltration, as demonstrated by Dr. Lynch, does not confirm this third possibility either.

It seems to me that there is a fourth possibility, namely, that plugging and atrophy of the follicle may prevent normal excretion of material, damming up material which normally passes into the follicular orifice from the cutis, that this material, impeded in its normal route and speed of excretion, may be gathered around the follicle, and that the reaction of the inflammation may be the reaction to the dammed-up fatty and other material which failed to find exit through the follicle. This hypothesis would explain many otherwise inexplicable observations in cases of acne vulgaris—for example, the exacerbations due to drugs, to certain foods and to glandular substances—and would also, in my opinion, account for the site of inflammation as found by Dr. Lynch.

I should like to ask Dr. Lynch's opinion of this fourth hypothesis.

DR. FRED D. WEIDMAN, Philadelphia. One feature of Dr. Lynch's presentation that interested me was the point he raised at the beginning, that it is difficult to distinguish between invagination of the surface and true hair follicles. A similar experience was encountered in a series of cases of trichoepithelioma which will be reported by Dr. H. J. Goldman. Dr. Goldman and I could find many condensations of keratinous material within the invaginations, but it was rare to

identify any hair shafts within them. The point of our studies was that, as the trichoepitheliomatous hyperplasias were taking place in connection with those invaginations, it was essential that we should make certain that the structures concerned were hair follicles before we could really call the hyperplastic structures trichoepitheliomas.

I have been wondering since then whether, on the face at least, there may be some invaginations occurring as part of an embryologic abnormality, the follicles never going on to full development and never leading to development of a hair shaft but remaining simply as invaginations. It may be that there are some of these which do not appear in the form of adenomatous trichoepitheliomas on the face but remain as hamartomatous structures and that they are the basis of these questionable hair follicles with which Dr. Lynch has been struggling.

Another feature in the presentation that interests me is the matter of the giant cell. I realize that Dr. Lynch was dealing only with the earlier phases of the pathogenesis of the acne lesion, but I must say that in some of the older lesions which I have studied there was no question about the stimulus to production of the giant cell. Of course, in cases in which the hair follicle had become destroyed its sheath was ruptured (there was suppuration) and within some of the giant cells it was possible to discover hair shafts. In other words, with rupture of the wall of the follicle the contents had attained an interstitial position round about and in the general mopping-up process foreign body giant cells were concerned.

Finally, I am always interested in the possibility that choline may provoke the inflammatory reaction. It has been known for many years that bacteria acting on lecithin will produce choline. Choline is a violent poison of an order of violence comparable to that of histamine. Every one is aware of the complexity of the lipid contents of acne lesions, whether early or late, and since lecithin is included among the lipoids, there is no reason why choline should not be present. I have several times remarked that probably every dermatologist is aware of the fact that when he squeezes out acne pustules the erythematous reaction round about seems to be out of all proportion to the trauma that has been inflicted. I wonder whether choline that has been liberated has diffused into the tissues.

Perhaps there is an easy way of testing that clinically. Thus, it is well known that atropine is the physiologic antidote for choline; accordingly, there is a means at hand of inquiring, at least in a superficial way, into the possible role of choline in provoking the earlier inflammatory phenomena of acne vulgaris.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I have not had the opportunity of studying the pathologic changes of early lesions of acne but have studied the histologic structure of severe types of acne, pyoderma faciale, etc. In the severe types of pyoderma one does not, as a rule, see a foreign body giant cell reaction unless there has been complete rupture or partial disintegration of the hair follicle. The concept expressed in some textbooks that there is a foreign body giant cell or even a tuberculoid type of reaction in cases of acne I think is a false one, and I am glad that Dr. Lynch has emphasized this.

In regard to the presence of micro-organisms, I have always felt there is a close association, in many cases, of acne with seborrhea of the scalp. The latter includes so-called seborrheic dermatitis. This is often associated with *Staphylococcus aureus* and with streptococci of different types, which I believe can be regarded as true pathogens and which probably are of some etiologic significance in these conditions, whether playing a primary or a secondary role.

DR. FRANCIS W. LYNCH, St. Paul: As several of the discussers pointed out, the later lesions of acne have quite a different appearance from the early lesions.

It is unfortunate that I have not yet been able to show how the early lesion leads to the later one and where or when the bacteria takes on significance. These studies do not allow me to make a positive suggestion as to the precipitating cause of the comedo, though some of the older theories receive no support from my studies.

As Dr. Montgomery indicated, the organisms observed in the sections have been found repeatedly on normal skin. Dr. Sulzberger's remarks on the reported absence of organisms from lesions on the back lead to several interesting lines of thought. Almost all of the bacteriologic studies in my cases were made of material from the face, but the sections of tissues were taken from the back in most instances, and organisms were found as in the facial lesions.

In connection with Dr. Weidman's mention of the frequent absence of the hair shaft, I am not sure of its significance. There must be many follicles which do not arrive at complete anatomic or, probably, physiologic development.

In addition to the chemical studies on choline which have been suggested, it might be profitable to work on the relation of butyric acid to the development of the acne lesion. Many of the staphylococci of acne form butyric acid in cultures, and it is possible that butyric acid is formed in the follicle, where it acts as an irritant.

I hope that my report has at least demonstrated that further histologic study of acne may not be fruitless.

LICHEN PLANUS OF THE NAIL BED

REPORT OF A CASE

GEORGE M. LEWIS, M.D.
NEW YORK

AND
J. F. RICCHIUTI, M.D.
MAHANOT CITY, PA.

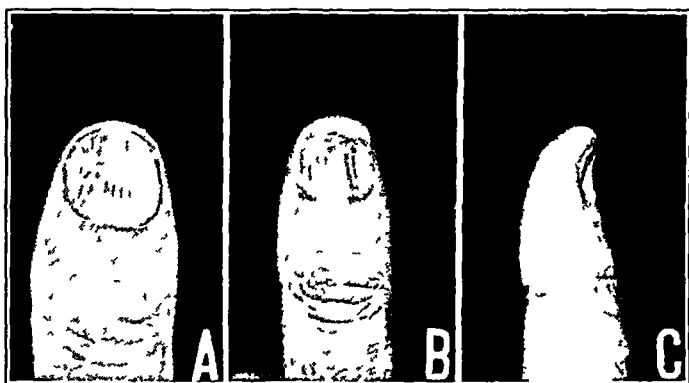
Pathologic changes in the nails of patients suffering from lichen planus have been reported by many observers. Most of the observations would seem not to be peculiar to lichen planus but to be indistinguishable from dystrophies of the nails secondary to some other diseases of the skin. Such abnormal changes in the nails as longitudinal and transverse striations, roughness or fragility, yellow or yellowish gray color, thinning, pitting, brittleness or fragility, yellowishness and opaqueness are and shedding have been described as due to lichen planus. Koilonychia has been reported following lichen planus. Heller¹ stated the belief that thickening, increased fragility, yellowishness and opaqueness are characteristic nail changes in lichen planus. Jadassohn² did not consider that changes of such character are pathognomonic of lichen planus. It is our opinion that such lesions when due to lichen planus are probably of indirect causation. In many instances the changes in the nails of patients with lichen planus may be purely coincidental. As against the considerable number of such instances of dystrophic changes in nails in patients with lichen planus, we have found only 7 recorded instances of lichen planus of the nail bed.

Although Heller³ credited de Lewin⁴ with reporting an instance of lichen planus of the nail bed, our study of the original report does not substantiate that opinion. We believe that the first authentic case is that described by Dubreuilh,⁵ whose patient had extensive lichen planus, with many punctate umbilicated papules at the bases of all the finger nails.

From the New York Hospital and the Department of Medicine (Dermatology), Cornell University Medical College.

1. Heller, J.: *Die Krankheiten der Nägel*, Berlin, A. Hirschwald, 1900, p. 144.
2. Jadassohn, J., cited by Heller.¹
3. Heller, J.: *Die Krankheiten der Nägel*, in Jadassohn, J.: *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1927, vol. 13, p. 222.
4. de Lewin, G.: *Ueber Keratosis universalis multififormis (Pityriasis pilaris rubra)* Besnier, *Lichen ruber acuminatus Kaposi*, *Berl. klin. Wchnschr.* **32**:801 and 829, 1895.
5. Dubreuilh, W.: *Lichen plan des ongles*, *Ann. de dermat. et syph.* **2**:606, 1901.

In the patient studied by Du Castel and Druelle ⁶ there were subungual papules visible through the transparent nail, as well as dystrophic changes, as evidenced by linear grooves and elevations. A similar instance of the disease affecting the nail bed was observed by Gaucher and Druelle ⁷. Gottheil ⁸ described the first case in the United States. In his patient all the finger nails and several toe nails were affected. The first lesion was a small flat black mark at the proximal portion of the lunula. This slowly moved distally. It increased in size from that of a pinpoint to that of a pinhead. There were also pressure atrophy, splitting of the nail and punctate depressions. In Vero's case, ⁹ papules were visible through the transparent nails of the index and middle fingers of both hands. Godrat ¹⁰ described a patient in whom all the finger nails showed elevations associated with pain and tenderness. There was associated softening of the nail, together with other changes. Sayer ¹¹ observed a patient with an extensive proved eruption of lichen planus, tiny



Lichen planus of the nail bed. *A*, typical violaceous papule. *B* and *C*, disappearance of the lesion following roentgen therapy, thinning of the nail plate with the formation of striae may be noted.

violaceous lesions could be seen through the nail plate arranged in parallel longitudinal lines. We question whether involvement of the nail bed is

6 Du Castel and Druelle. Alterations des ongles chez un malade atteint de lichen plan, *Bull Soc franç de dermat et syph* **14** 246, 1903.

7 Gaucher and Druelle. Lichen plan avec lesions des ongles et localisation sur la conjonction palpebrale, *Bull Soc franç de dermat et syph* **115** 33, 1904.

8 Gottheil, W S. Lichen Planus Unguium, *J Cutan Dis* **27** 317, 1909.

9 Vero, F. Lichen Planus of the Nails. Report of a Case, *Arch Dermat & Syph* **26** 677 (Oct) 1932.

10 Godrat, M J. Lichen plan des ongles, *Bull Soc franç de dermat et syph* **41** 777, 1934.

11 Sayer, A. Generalized Lichen Planus with Lesions of the Palms and Nails, *Arch Dermat & Syph* **41** 813 (April) 1940.

as rare as the few cases reported would indicate. However, Little¹² stated the belief that the nails are seldom involved.

REPORT OF CASE

J. F. R., a physician aged 33, noticed during the summer of 1938 a dime-sized elevated, reddish brown plaque, which was not pruritic, over the right tibia. This remained as a solitary lesion. In April 1939 he noticed on the legs several flat-topped, violaceous, moderately itchy papules. A little later similar lesions appeared on the flexor surfaces of the forearms. There were no lesions on the mucous membrane of the mouth, but a small lesion was noted on the glans penis. The Wassermann reaction was negative; a hemogram was normal, and the urine showed no pathologic changes. The diagnosis of lichen planus was indisputable. He was given pills containing $\frac{1}{8}$ grain (8 mg.) protiodide of mercury and took these three times daily. Treatment was suspended after a week because of moderate diarrhea thought to be due to the medication. During the summer of 1939 most of the lesions disappeared spontaneously. In August a violaceous papule appeared on the nail bed of the left thumb within the lunula. The papule was irregularly rectangular in shape and four months after its appearance occupied a third of the nail. As the lesion grew, the nail plate over it became thinned. Pain was experienced on moderate pressure. The nail plate distal to the lesion showed longitudinal striae. The patient was presented before the Manhattan Dermatologic Society¹³ in November, and most of the members agreed that the lesion of the nail bed was a typical papule of lichen planus. Treatment was started in November by the administration of unfiltered roentgen rays. Three unfiltered exposures of 150 r each were given at intervals of two weeks. A fourth treatment consisted of 75 r filtered with 1 mm. of aluminum. The lesion at first became flatter but continued to increase in diameter. After the third treatment definite regression was apparent, and by February 1940 the lesion had disappeared. The entire nail plate showed longitudinal striae and was of less than normal thickness. No pain was noted on pressure.

SUMMARY AND CONCLUSION

An instance of lichen planus involving the nail bed is reported, the eighth on record.

The lesion responded to roentgen therapy.

Dystrophic changes of the nails in patients with lichen planus are not pathognomonic of that disease.

121 East Sixtieth Street.

228 West Mahanoy Avenue.

12. Little, E. G.: Lichen Planus, *J. Cutan. Dis.* **37**:639, 1919.

13. Lewis, G. M.: Lichen Planus of the Nail Bed, *Arch. Dermat. & Syph.* **41**:947 (May) 1940.

XC—MICROSPOROSIS OF THE SCALP CAUSED BY MICROSPORUM FULVUM

REPORT OF A CASE AND DESCRIPTION OF THE FUNGUS

MORRIS MOORE, PH D

Mycologist to the Barnard Free Skin and Cancer Hospital, the Barnes Hospital
and the Washington University School of Medicine

AND

ADOLPH H CONRAD JR, M D

Resident in Dermatology

ST LOUIS

The infrequency of microporosis due to *Microsporum fulvum* in the United States, and particularly in the midwest, warrants the report of the following case

REPORT OF CASE

N R, a boy aged 4 years, entered the dermatologic clinic of the Barnard Free Skin and Cancer Hospital on Dec 19 1939, with a "sore on the scalp," which, the child's mother stated, had been present for a week and showed a gradual increase in size

Examination showed a circular patch of dermatitis with some alopecia and short broken-off hairs (fig 1) The involved area was mildly hyperemic, slightly raised above the surface of the surrounding skin and approximately 3.5 cm in diameter The lesion consisted of discrete and confluent papules, which were covered with grayish scales

Scrapings from the lesion and some of the short, broken-off hairs were examined microscopically They showed filaments and chains of spores, particularly the freshly infected hairs and scrapings from the periphery of the lesion (fig 2) Hairs from the central area of the lesion showed a sheath of spores which was analogous to that produced by the microsporum Cultures on Sabouraud's maltose and dextrose agars confirmed the presence of a microsporum, *M fulvum*

The source of infection could not be determined in this case, since there were no pet animals in the house, although there were many in the neighborhood Two other children in the family, one younger and one older, were free from the infection

The patient was given an ointment of salicylic acid (5 per cent) and precipitated sulfur (10 per cent) in petrolatum to apply three times daily He failed to return to the clinic An investigation four months later revealed that because of financial reasons the boy, on December 30, had been taken to the St Louis City Hospital, which was in the vicinity of his home At that institution he was given a similar ointment On Jan 2, 1940 the lesion was described as an "inflammatory

Studies, observations and reports from the Departments of Dermatology and Mycology of the Barnard Free Skin and Cancer Hospital, service of Dr M F Engman Sr

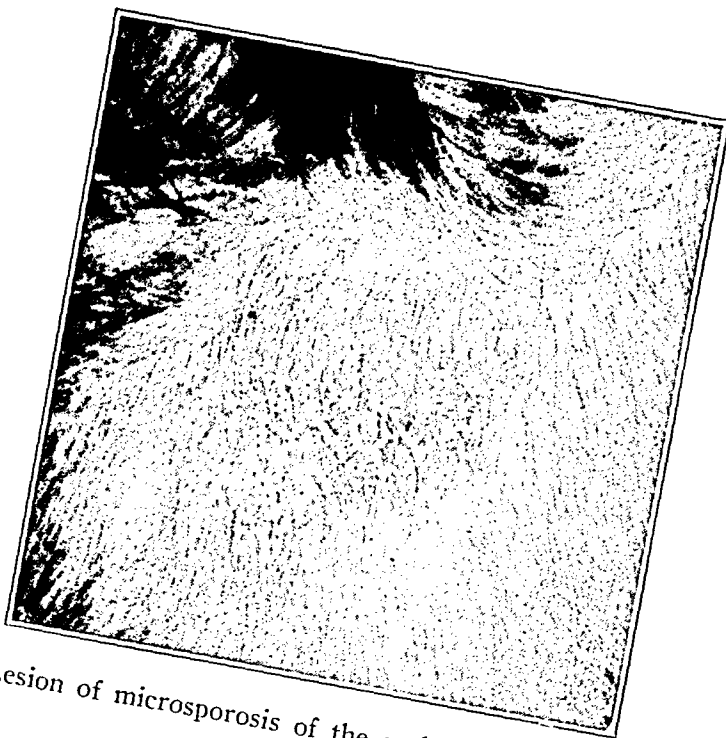


Fig. 1.—Lesion of microsporiasis of the scalp caused by *M. fulvum*.

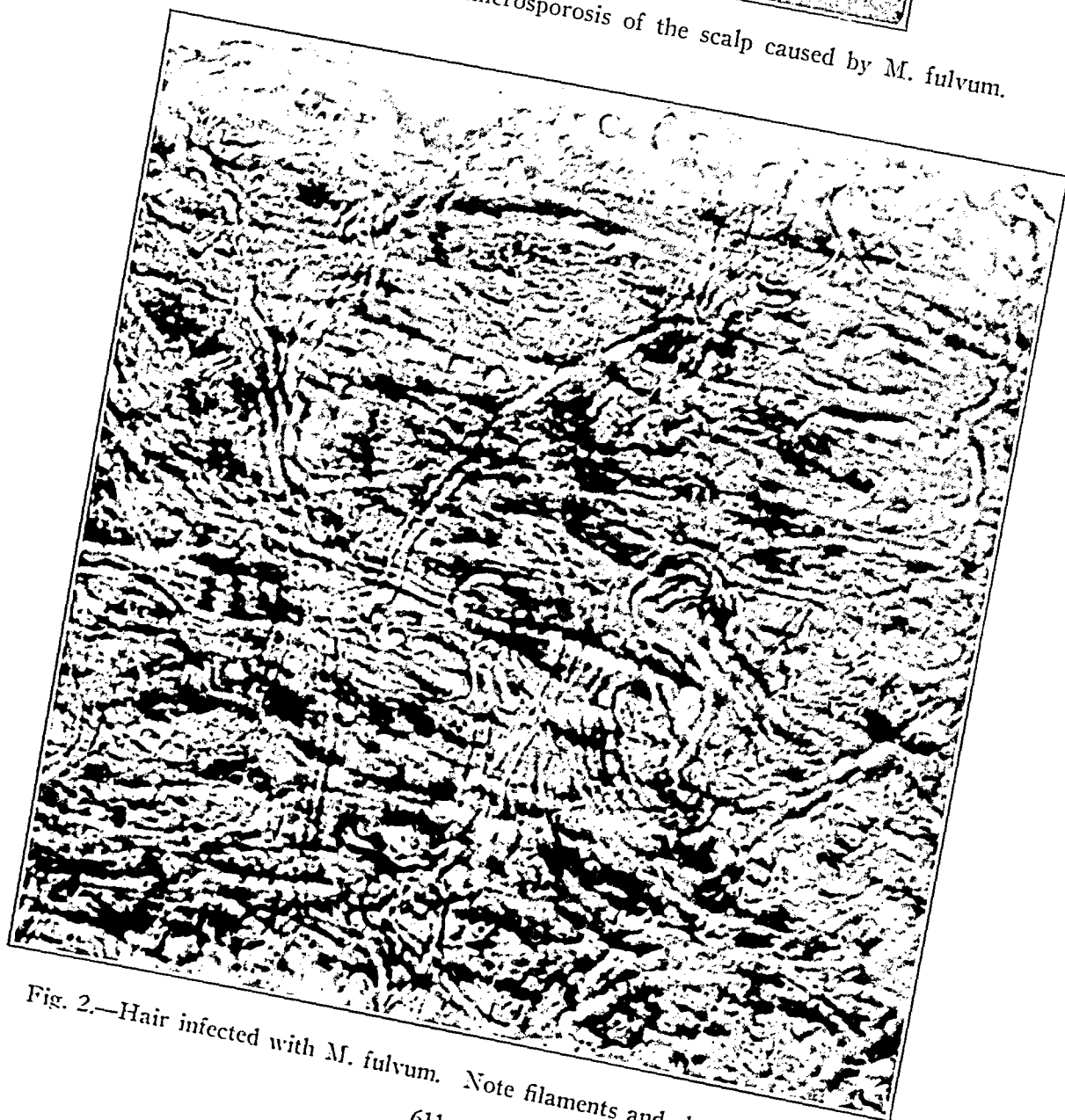


Fig. 2.—Hair infected with *M. fulvum*. Note filaments and chains of spores.

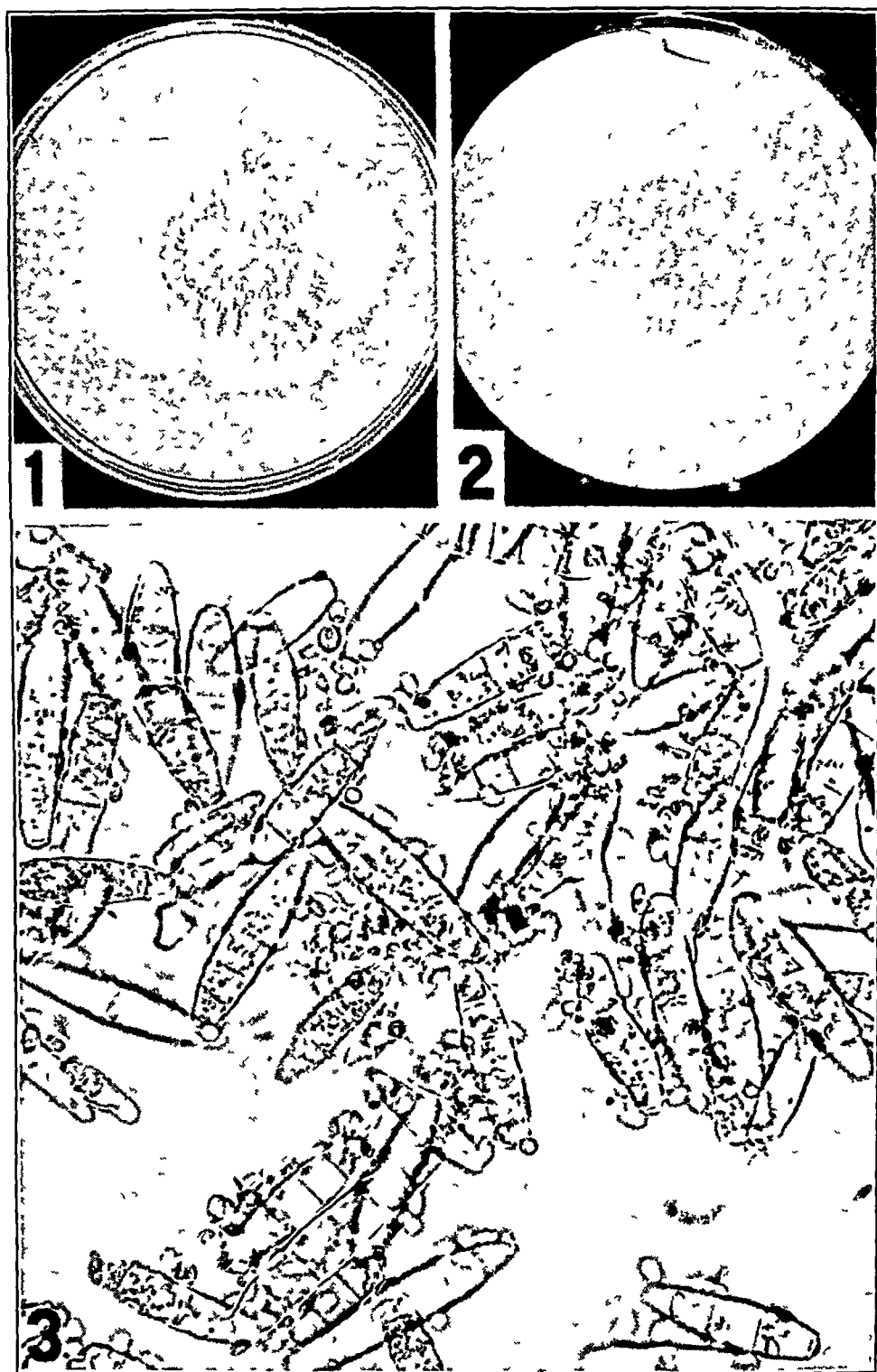


Fig 3—1, sixteen day old growth of *M. fulvum* on Sabouraud's glucose agar 2, sixteen day old growth of *M. fulvum* on Sabouraud's maltose agar 3, fuseaux and microconidia or aleurospores of *M. fulvum* grown on Sabouraud's maltose agar (× 560)

dermatitis of the scalp," and wet packs of mercury bichloride (1:5,000) and the subsequent application of ammoniated mercury ointment (5 per cent) were prescribed. The mother was advised to epilate all remaining broken-off hairs. The wet packs were discontinued on January 4. The patient was last seen on January 13, at which time the dermatitis was rapidly clearing. By April 4, the lesion had completely disappeared, and the area was covered with apparently healthy hair.

Microsporosis due to *M. fulvum* was first described by Uriburu¹ in 1909 in Argentina, where it was reported as being fairly common. The organism has also been described in reports from Uruguay, Brazil, Germany, Hungary and Canada and in a few from New York. Clinically, microsporosis due to *M. fulvum* may resemble closely an early patch of favus. Microscopically the fungus on the infected hair may simulate microsporums of animal origin or at times *Achorion schoenleini*. Although no direct evidence is available, *M. fulvum* is generally considered to be transmitted by dogs or cats.

In culture *M. fulvum* grows rapidly, producing a characteristic growth in sixteen days. A white central umbo is formed, surrounded by a powdery, ochraceous buff, pinkish buff to light cinnamon-colored velvet, which in turn may be surrounded by an irregular, white, cottony growth, as on Sabouraud's dextrose agar (fig. 3, 1). On Sabouraud's maltose agar after sixteen days a growth of concentric rings is formed (fig. 3, 2). The cultural growth may become rapidly pleomorphic, as evidenced by the formation of white, cottony tufts.

Microscopically the cultural growth shows a large number of multi-septate fuseaux (macroconidia or clostero-spores), which are usually four to six celled, measuring approximately 30 to 55 by 10 to 15 microns, ellipsoid and thin walled, with warty excrescences on the surface. The fuseaux may be found in groups of twelve to fifteen on branched conidiophores (fig. 3, 3). Microconidia or aleurospores are also evident. These measure approximately 2 to 4 by 3 to 5 microns and are spherical or ovoid, sessile or on short sterigmata. On Sabouraud's sugar mediums there also may be seen chlamydo-spores, arthrospores, nodular bodies, pectinate hyphae and spirals.

This organism at times may be confused with the common microsporums of animal origin, particularly *Microsporum canis* and *Microsporum felineum*, and should be differentiated in order to demonstrate that this organism is not as rare as is supposed.

1. Uriburu, J. V.: Contribución al estudio de las tinias en Buenos Aires, Argent. méd., 1909, no. 42, p. 241; no. 43, p. 258; no. 44, p. 260; cited by Dodge, C. W.: Medical Mycology, St. Louis, C. V. Mosby Company, 1935, p. 541, and Sabouraud, R.: Les teignes, Paris, Masson & Cie, 1910.

EXTENSIVE LICHENIFIED ERUPTION CAUSED BY TRICHOPHYTON RUBRUM

JACOB H SWARTZ, M D

Associate in Dermatology, Harvard Medical School

BOSTON

AND

NORMAN F CONANT, P H D

DURHAM, N C

The purpose of this paper is to report 4 cases, 2 in detail, of extensive lichenified dermatitis caused by *Trichophyton rubrum* (Castellani 1910, Sabouraud 1911), an organism rarely found in this part of the country. While Ota¹ has shown this organism to be frequently the cause of "eczema marginatum" in Japan and Manchuria, Weidman² in a discussion of the geographic distribution of *T. (purpureum) rubrum* showed not only that it was frequently found in Japan and Manchuria but that it was also common in the southern part of the United States. Hodges³ also reported finding this fungus in cases of eczema marginatum, onychomycosis and dermatitis interdigitalis in the south. From New York, Lewis, Montgomery and Hopper⁴ have recently reported on it in dermatoses simulating arsenical keratosis, neurodermatitis, eczema, sycosis vulgaris and erythema annulare centrifugum. The organism reported by the latter authors appears to be similar to the one found in the cases to be reported here.

Read at the Third International Congress for Microbiology, New York, Sept 8, 1939

From the Department of Dermatology, Massachusetts General Hospital, Boston, and from the Department of Bacteriology, Duke University School of Medicine, and Duke Hospital, Durham, N C. The work at Duke Hospital was aided by a grant from the John and Mary R Markle Foundation.

1 Ota, M. Contribution to the Study of *Trichophyton Purpureum* Bang, *Trichophyton Interdigitale* Priestly and *Trichophyton B* Hodges, also on *Trichophyton "A"* and *Trichophyton "B"* of Author, *Arch Dermat & Syph* 5 693-713 (June) 1922

2 Weidman, F D. Laboratory Aspects of Epidermophytosis, *Arch Dermat & Syph* 15 415-450 (April) 1927

3 Hodges, R S. Ringworm of the Nails, *Arch Dermat & Syph* 4 1-26 (July) 1921

4 Lewis, G M, Montgomery, R M, and Hopper, M E. Cutaneous Manifestations of *Trichophyton Purpureum* (Bang), *Arch Dermat & Syph* 37 823-839 (May) 1938

REPORT OF CASES

CASE 1.—Mrs. E. O., aged 37, white, reported to the Massachusetts General Hospital in March 1935, complaining of an extensive eruption involving the upper and lower extremities of six years' duration. The lesions first appeared on the right foot and then extended upward to the knee. Involvement of the right arm was noticed four years later. Itching was severe.



Fig. 1.—Extensive eruption on the shoulder, with sharply demarcated border. Lesion consists chiefly of lichenified papules.

Examination of the skin showed an extensive eruption involving the right upper extremity from shoulder to finger nails (fig. 1). Both the extensor and the flexor aspects were involved. A similar extensive eruption was noticed also on the right lower extremity, extending from the knee downward and including the toe nails, which were discolored yellowish brown and deformed. The eruption consisted chiefly of lichenified papules, some covered with scales, with a sharply demarcated border. The center areas showed tendency to clearing. The lower part of the trunk, the chest and the suprapubic regions showed pinhead-sized lichenified papules with a tendency toward follicular distribution. Some of the

areas which had cleared showed depigmentation, surrounded by a zone of hyperpigmentation. These simulated areas of tinea versicolor after exposure to the sun.

This eruption was resistant to all forms of local treatment except the following ointment:

Chrysarobin	2 per cent
Salicylic acid	6 per cent
Precipitated sulfur	6 per cent
Petrolatum	1 ounce (31 Gm)

This ointment, however, was helpful only up to a certain point, and then improvement of the condition remained at a standstill. Inhalations of ethyl iodide proved the most effective form of therapy in this case.

CASE 2—Mrs. N. V., aged 28, white, entered the Massachusetts General Hospital on Nov. 11, 1938, with a complaint of extensive itching. She was well up to one and one-half years ago except for ichthyosis, which required only the application of some cream during the winter. About the time of onset the patient noticed a few "blister-like" spots which appeared on the proximal dorsal aspects of the toes with a spread down to the webs. This was accompanied by pruritus. The interdigital spaces were fissured. About two to three months after this she noticed small "blister-like" lesions on the thighs and chest. Soon more appeared on the thighs, chest and back (fig. 2).

The examination of the skin showed many circular and gyrate lesions, some small and some rather large, scattered over the legs, trunk and arms. The borders were slightly raised and composed of fine lichenified, scaly papules. The centers were clear. Intermingled with these lesions were lichenified plaques varying in size. The skin also showed typical ichthyosis. No evidence of any vesicles was noted.

The eruption was resistant to all forms of local treatment but responded to inhalations of ethyl iodide.

Previous reports⁵ have been interpreted as advocating inhalations of ethyl iodide for all types of fungous infections. Although several types of fungous infection have been treated by this method, it should be noted that the cases were selected "because of extensive involvement, long duration of the disease or lack of response to other forms of treatment." In systemic infections, dermatophytosis of the groins or intergluteal fold and extensive invasion of the skin, as in the cases being presented, the use of inhalations of ethyl iodide has proved to be the most effective method of treatment.

STUDY OF THE ETIOLOGIC AGENT

In case 1 material for study was taken, by means of a curet, from several places in the involved areas. Scrapings were taken from the

⁵ Swartz, J. H., Blumgart, H. L., and Altschule, M. D. Ethyl Iodide Inhalations in the Treatment of Mycotic Infections of the Skin and Allied Conditions, *Arch. Dermat. & Syph.* **21**: 182-185 (Feb.) 1930. Swartz, J. H., and Reilly, M. Inhalations of Ethyl Iodide in Fungous Infections, *ibid.* **32**: 551-555 (Oct.) 1935.

infected toe nails, from the interdigital spaces on the foot and from the border of the lesion on the calf. Likewise, scrapings were taken from the lesion involving the arm, from the border of the lesion at the shoulder and at four intervals along the arm to the fingers. These bits of skin and scrapings were examined microscopically after being treated with 15 per cent potassium hydroxide, and each showed a network of branch-



Fig. 2.—Circular and gyrate lesions, with borders slightly raised, composed of fine lichenified papules and scaling.

ing mycelium, characteristic of fungous invasion (fig. 3). Examination of material taken from the involved areas in the other cases also showed an identical extensive fungous invasion of the skin. Identification of the organism responsible for these lesions was made by a cultural and morphologic study of the fungus obtained from the infected material.

Cultural Study of the Fungus.—Small pieces of material obtained from the lesions were planted on Sabouraud's dextrose agar. After four

days at room temperature, each bit of inoculum sent out a radiating mycelial growth onto the agar. In a week the center of each growth was purple, owing to the formation of pigment in the agar. The cultures

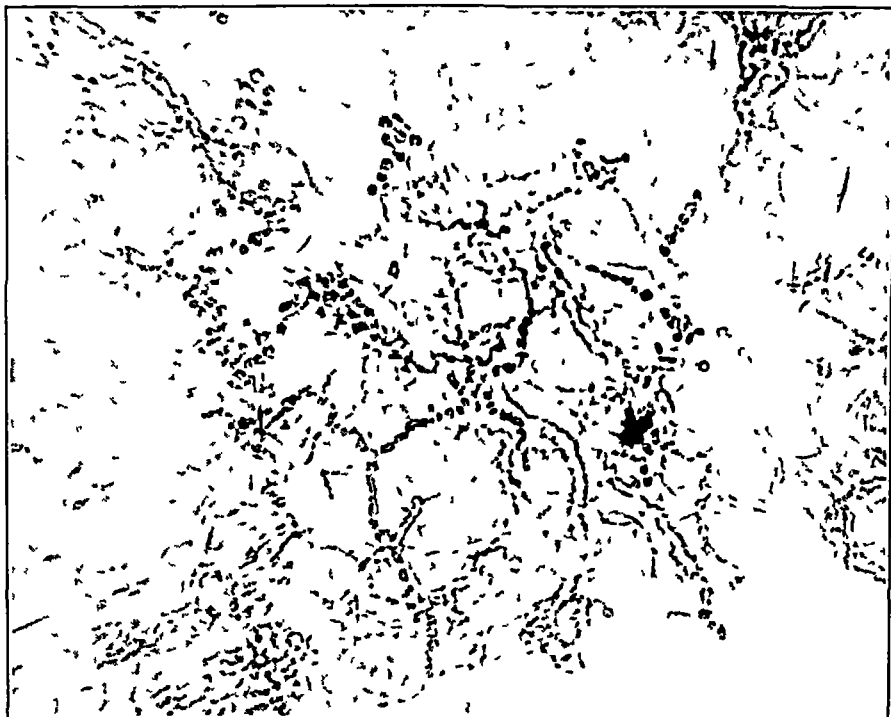


Fig 3—Invasion of skin by a branching network of mycelium. The hyphae have broken up into oblong segments. Other preparations showed continuous unbroken hyphae.

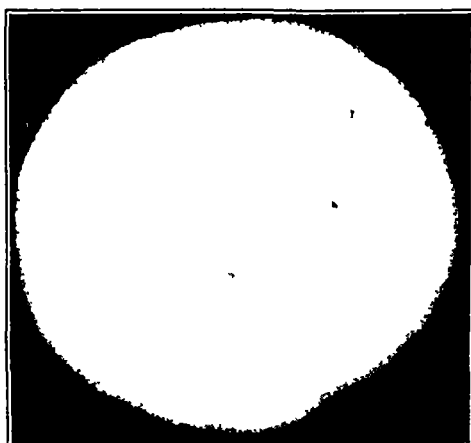


Fig 4—Culture of *T. rubrum* after three weeks on Sabouraud's dextrose agar (natural size).

at this time were close growing with little aerial mycelium and appeared moist around the periphery. After ten days, however, an aerial mycelium developed in the center of the colonies, giving a loose cottony appearance,

while the border of the colonies sloped off to the agar, forming a wide moist band around each growth. The purplish color noticed in the early cultures was readily seen around the periphery of these ten day growths. The central aerial mycelium, however, hid the color, but on the reverse side of the cultures the pigmentation was readily noticeable and was deep purple. After ten days the aerial mycelium lost its cottony character, giving way to a white powdery type of growth. This aerial powdery growth became pinkish in older cultures, while the pigmentation in the medium remained purple (fig. 4).

Transfers from the old pigmented cultures to fresh mediums showed a tendency to lose the purple pigmentation. The ability to produce any pigmentation was completely lost after three transfers. These cultures showed a raised center with close growing white aerial mycelium. The peripheries of these cultures were close growing and waxlike in appearance.

Morphologic Study of the Fungus.—A study of the morphology of the fungus isolated from these cases was made in the following way: First, material was taken from tube and plate cultures and carefully teased and mounted in lactophenol cotton blue; secondly, Van Tieghem cell cultures were made, and the fungus was studied in its living condition.

In stained preparations the pinkish powdery centers of the month old cultures were found to be almost entirely made up of microconidia. These small single-celled subspherical spores, because of their great numbers, were responsible for the powdery character of the cultures. While these microconidia were produced laterally along the slender hyphae in some cases (fig. 5, 5), frequently side branches also bore the small conidia. In the type of growth in which side branching occurred, the conidia were closely arranged and gave the appearance of being borne in clusters (fig. 5, 1).

A reproductive body different from the aforementioned single-celled microconidia was also found in cultures of this fungus. This spore was the typical macroconidium (fuseau) of the genus *Trichophyton*. This macroconidium was elongated, club shaped, clavate and multicellular, with thin smooth walls. It was bluntly rounded at the apex and had a broad base (fig. 5, 4). These large conidia were borne in the mycelium of the cultures as terminal elements of blown-up or expanded ends of hyphae. There were at first few septums, but gradually others were laid down, and the general appearance of the enlarged, swollen apical portion of the hypha became that of the typical macroconidium or fuseau. Although a study of stained material helps to identify fungi, a study of the fungus in its living condition should be attempted. This can best

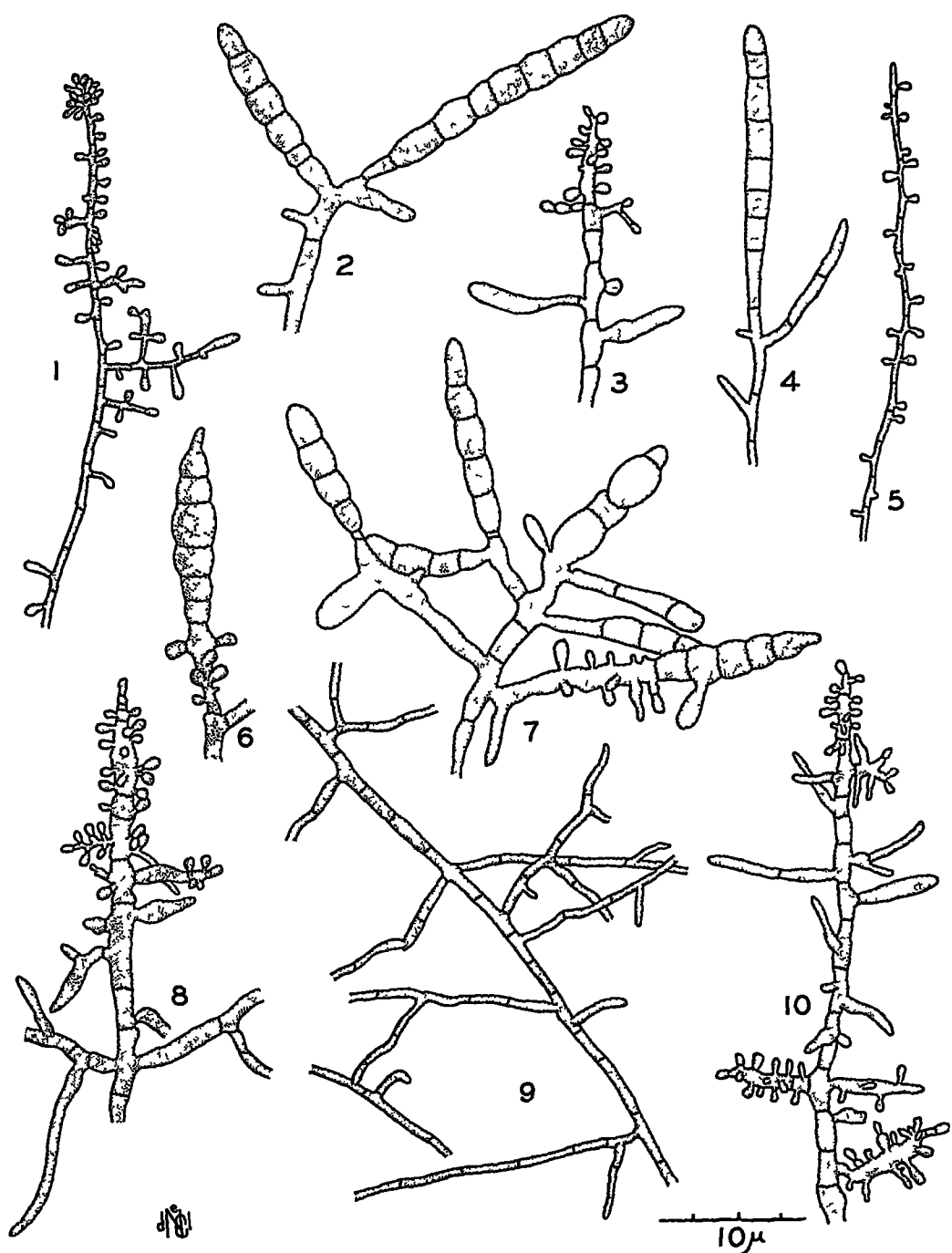


Fig 5—All drawings were made with the aid of a camera lucida ($\times 558$) 1 and 5, microconidia borne laterally and on side branches of slender hyphae 2, 6 and 7, large swollen terminal structures seen in the medium of cell cultures 3, 8 and 10, swollen mycelium branches with microconidia seen in the medium of cell cultures 4, typical macroconidium (fuseum) in aerial mycelium 9, slender anastomosing mycelium

be accomplished by studying the development of the organism in cell cultures. Spring,⁶ however, has found that several cell cultures of a single ringworm fungus should be studied to account for the morphologic variations which occur in a single species. For this reason, ten cell cultures were made and examined over a period of one month. Microconidia and fragments of hyphae germinated and produced a weft

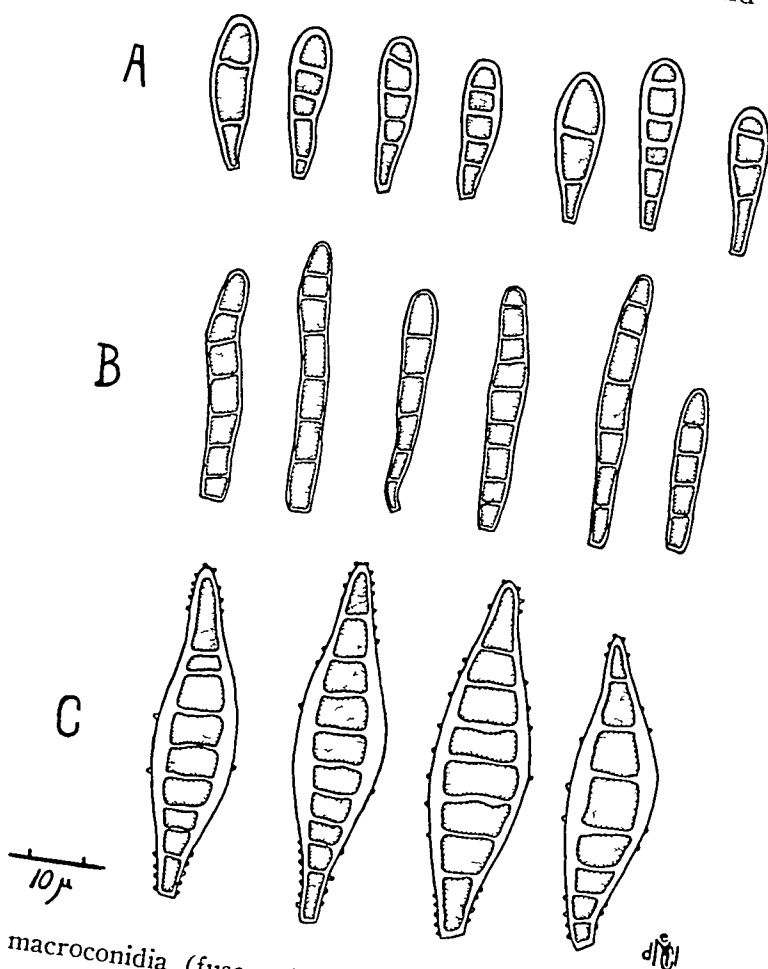


Fig. 6.—A, macroconidia (fuseaux) of the genus *Epidermophyton*. B, macroconidia of the genus *Trichophyton*. C, macroconidia of the genus *Microsporon*.

of slight, isodiametric, anastomosing mycelium (fig. 5, 9). Occasionally portions of the mycelium became enlarged and swollen with cells of irregular diameter (fig. 5, 2, 6 and 7). These enlargements, occurring in the medium, became septate, with constrictions at each septation, giving the appearance of macroconidia. Other portions of the hyphae which became enlarged bore small single-celled microconidia along their swollen branches (fig. 5, 3, 8 and 10).

6. Spring, D.: Morphologic Variation Within the Same Species of Dermatophyte as Observed in Hanging-Drop Cultures, *Arch. Dermat. & Syph.* **23**:1076-1086 (June) 1931.

While other structures serve to help distinguish genera among the dermatophytes, the macroconidium is, perhaps, the most useful. Three types of these large spores distinguish the genera *Trichophyton*, *Microsporon* and *Epidermophyton* (fig 6, *A*, *B* and *C*). The macroconidia of the genus *Epidermophyton* have two or more septums, are oval to obovate in shape and have a relatively thin and smooth wall (fig 6, *A*). These differ from the macroconidia of *Trichophyton*, which are elongated, clavate, multiseptate and bluntly rounded at the apex and have a thin and smooth wall (fig 6, *B*). The macroconidia of the genus *Microsporon* differ from the other two kinds in that they are multiseptate, spindle-shaped, pointed at the apex and narrowed to a broad base. The walls of these macroconidia are thick at the median cells and roughened at least at the extremities (fig 6, *C*). These three types of macroconidia, then, clearly separate the genera of the dermatophytes by presenting differences in such distinct morphologic features as size, shape and character of the walls. The macroconidia borne in the aerial mycelium of our fungus were seen infrequently in the cell cultures on Sabouraud dextrose slants. They were found in greater number, however, on sterilized polished rice in flask cultures (fig 6, *B*).

e
COMMENT

The fungus herein described was identified as belonging to the genus *Trichophyton* because of the typical macroconidia it produced when cultured on the standard mediums and on polished rice. The purplish pigmentation on the reverse side of the cultures and the pinkish color of the aerial mycelium would allow this fungus to be identified as one of several species to be found described in the literature. The fungus, however, lost its ability to produce pigment after two transfers. It is this tendency to lose characteristic cultural reactions which makes identification of the dermatophytes difficult.

Not only did this fungus vary in its gross cultural characteristics, but it showed a great variation in the production of microscopic characters. On Sabouraud's dextrose medium, for example, macroconidia were produced irregularly. At times it was necessary to examine cultures exhaustively before the large conidia could be found. However, it was found that the large conidia, characteristic of the genus *Trichophyton*, were produced in great numbers on polished rice in flasks. This is as Langeron and Milochevitch⁷ found for the dermatophytes as a group, i. e., in cultures on natural mediums (grains of barley, wheat and rye) spore forms were produced in greater number and more frequently than

⁷ Langeron, M., and Milochevitch, S. Morphologie des dermatophytes sur milieux à base de polysaccharides. Essai de classification, *Ann de parasitol* 8 465-508, 1930.

in cultures on the standard agar mediums. Such irregularity of the formation of diagnostic structures in cultures adds to the difficulty of identifying the dermatophytes.

A further complication in identification of these fungi is the non-specificity in the type of lesion they may produce. That the same fungus may cause several different types of lesions or that the same lesion may be caused by different fungi has been stressed in the literature for years. In this respect, Langeron and Milochevitch⁷ and Grigorakis⁸ have pointed out the various clinical manifestations produced by the same fungus or by different fungi.

Because of these cultural, morphologic and clinical variations several species of *Trichophyton* have been described with which the fungus being reported may be identified. Recently Ota and Kawatsur⁹ made a critical study of several of these similar fungi, showed them to be variations of one species and reduced to synonymy with *Sabouraudites ruber* (Castellani; Ota and Langeron 1923) seventeen variously named species. *Sabouraudites ruber*, however, was a new name for a species which Castellani¹⁰ had named *Epidermophyton rubrum* in 1910. This was changed by Sabouraud,¹¹ however, to *T. rubrum* in 1911. At this time Sabouraud acknowledged the priority of Castellani's fungus to that of Bang.¹² *Trichophyton purpureum*, which had been discovered and worked on by Bang in Sabouraud's laboratory. From a review of the literature it would seem that the synonymy of this group of fungi producing a red to purplish pigmentation should be as shown in the following tabulation:

Epidermophyton rubrum Castellani, Brit. J. Dermat. **22**:147-150, 1910.

Epidermophyton Perneti Castellani, Brit. J. Dermat. **22**:147-150, 1910.

Trichophyton purpureum Bang, Ann. de dermat. et syph. **1**:224-238, 1910.

Trichophyton rubrum (Castellani) Sabouraud, Brit. J. Dermat. **23**:375-402, 1911.

Trichophyton rubidum Priestley, M. J. Australia **2**:474, 1917.

Epidermophyton salmonicum de Mello, Compt. rend. Soc. de biol. **84**:239-240, 1921.

Trichophyton A Hodges, Arch. Dermat. & Syph. **4**:1-26 (July) 1921.

8. Grigorakis, L.: (a) Recherches cytologiques et taxonomiques sur les dermatophytes et quelques autres champignons parasites, Ann. d. sc. nat. (Botan.) **7**:165-444, 1925; (b) Dermatophytes et dermatomycoses, Ann. de dermat. et syph. **10**:18-53, 1929.

9. Ota, M., and Kawatsur⁹, S.: Sur le *Sabouraudites ruber* et ses variétés, Ann. de parasitol. **11**:476-501, 1933.

10. Castellani, A.: Observation on a New Species of *Epidermophyton* Found in *Tinea Cruris*, Brit. J. Dermat. **22**:147-150, 1910.

11. Sabouraud, R.: Eczematoid Ringworm of the Extremities and Groins: II, Brit. J. Dermat. **23**:375-402, 1911.

12. Bang, H.: Sur une trichophytie cutanée à grand cercles, causée par un dermatophyte nouveau (*Trichophyton purpureum*, Bang), Ann. de dermat. et syph. **1**:225-238, 1910.

- Trichophyton B* Hodges, Arch Dermat & Syph **4** 1-26 (July) 1921
- Trichophyton marginatum* Mujs, Nederl tijdschr v geneesk **65** 2205-2207, 1921
- Sabouraudites ruber* Ota and Langeron, Ann de parasitol **1** 328, 1923
- Trichophyton lilcum* Kawasaki, Jap J Dermat & Urol **23** 940-964, 1923
- Trichophyton purpureum* var *I* Takahashi, Jap J Dermat & Urol **25** 251-286, 1925
- Trichophyton purpureum* var *II* Takahashi, Jap J Dermat & Urol **25** 251-286, 1925
- Epidermophyton plurizonforme* MacCarthy, Ann de dermat et syph **6** 31-37, 1925
- Epidermophyton lanosolum* MacCarthy, Ann de dermat et syph **6** 49-53, 1925
- Trichophyton coccineum* Katoh, Tr Sixth Cong Far East A Trop Med, Tokyo, 1925, pp 861-865
- Bodinia spadicea* Katoh, Tr Sixth Cong Far East A Trop Med, Tokyo, 1925, pp 865-866
- Trichophyton multicolor* Magalhães and Neves, Mem Inst Oswaldo Cruz **20** 271-298, 1927
- Sabouraudites plurizonformis* Brumpt, Precis de parasitologie, ed 4, Paris, Librairie de l'Académie de Médecine, 1927, p 1291
- Sabouraudites ruber* var *blanche* Hashimoto, Irizawa and Ota, Jap J Dermat & Urol **30** 243-251, 1930
- Bodinia spadicea* Pollacci and Nannizzi, I miceti patogeni dell'uomo e degli Animali, Siena, S A Poligrafica Meini, vol 10, no 91
- Trichophyton Kagawaense* Fujii, Jap J Dermat & Urol **31** 305-357, 1931
- Sabouraudites ruber* var *III* Fujii, Jap J Dermat & Urol **32** 575-584, 1932
- Trichophyton coccineum* var *Leio* Nakamura, Jap J Dermat & Urol **32** 515-527, 1932
- Epidermophyton purpureum* Dodge, Medical Mycology, St Louis, C V Mosby Company, 1935, p 485
- Ectotrichophyton Otac* Dodge, Medical Mycology, St Louis, C V Mosby Company, 1935, p 500
- Favotrichophyton coccineum* Dodge, Medical Mycology, St Louis, C V Mosby Company, 1935, p 524
- Favotrichophyton violaceum* var *marginatum* Dodge, Medical Mycology, St Louis, C V Mosby Company, 1935, p 524

SUMMARY

Four cases of severe dermatophytoses causing an extensive lichenified eruption are reported. Two are described in detail.

Resistance to local treatment was uniform except that one ointment, consisting of 2 per cent chrysarobin, 6 per cent salicylic acid and 6 per cent precipitated sulfur in petrolatum, caused a limited amount of improvement.

Inhalations of ethyl iodide were of definite value and proved to be the most effective form of therapy in this type of case.

A cultural and morphologic study of the etiologic agent in these cases established *T. rubrum* (Castellani, Sabouraud 1911) as the causative fungus.

The probable synonymy of this species includes several fungi which produce a red to purplish pigmentation in culture.

THE MICROPAPULAR TUBERCULID

CARL W. LAYMON, M.D.

AND

HENRY E. MICHELSON, M.D.

MINNEAPOLIS

Micropapular tuberculid is the term which we have applied to a form of cutaneous tuberculosis composed of tiny papules occurring on the face. This type, while differing from both lupus miliaris disseminatus faciei and acnitis, may at times resemble rosacea.

Tuberculoderms, although subject to great clinical variations, have a fairly well established course and prognosis, especially in a specific case in which the characteristics conform strictly to a well recognized type of cutaneous tuberculosis. This is true of lupus vulgaris, lupus miliaris disseminatus faciei and acnitis. There are, however, patients on whom lesions are found, particularly on the face, which have a prolonged course and a tuberculoid structure but still do not conform morphologically to any of the aforementioned types.

Lewandowsky¹ in 1917 first described such a type of tuberculosis of the skin, which he called rosacea-like tuberculid. His classic description is now well known and has been reintroduced by the articles of MacKee and Sulzberger² and Wile and Grauer.³

We believe that the condition of patients having an eruption of the face consisting of small papules so arranged that they give the casual appearance of rosacea is often diagnosed as rosacea-like tuberculid when a careful analysis might reveal that the eruption belongs to some other type of tuberculosis, such as lupus miliaris disseminatus faciei, acnitis or even papular sarcoid. As is often the case in medical circles, a diagnosis is popularized without strict adherence to the criteria for the diagnosis. We believe that this is the case with rosacea-like tuberculid. We think that the term is objectionable and that it leads to mistaken diagnoses, for in all probability many lesions of resistant rosacea have been called tuberculous.

Read at the Sixty-Third Annual Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., May 30, 1940.

1. Lewandowsky, F.: Ueber rosacea-ähnliche tuberkulide des Gesichtes, *Cor.-Bl. f. Schweiz. Aerzte* **47**:1280, 1917.

2. MacKee, G. M., and Sulzberger, M. B.: Rosacea-Like Tuberculid of the Face, *Arch. Dermat. & Syph.* **31**:159 (Feb.) 1935.

3. Wile, U. J., and Grauer, F. H.: Rosacea-Like Tuberculosis, *Arch. Dermat. & Syph.* **31**:174 (Feb.) 1935.

In order to adhere strictly to a concept one must define the appearance, course and healing of a tuberculid. In our opinion, the tuberculid is the most characteristic cutaneous manifestation of internal tuberculosis, and it should be looked on as a transient projection of the disease on the skin. The appearance and disappearance of tuberculids, therefore, must have to do with factors that control dissemination of the tubercle bacilli from their original focus. On the other hand, lesions in the skin



Fig. 2.—Mr. D. A., aged 20. The duration of the eruption was two months. The lesions were tiny reddish brown papules on the forehead, nose, cheeks and chin. The eruption did not resemble rosacea. Physical examination showed no visceral tuberculosis. The Mantoux reaction (1:1,000) was weakly positive. After six months of treatment, including roentgen irradiation, administration of gold sodium thiosulfate and generalized ultraviolet irradiation, the eruption disappeared completely and has not recurred in four years.

that possess undoubted characteristics of lupus must signify that the bacilli, having reached the skin, find it so receptive for the particular type of inflammation called lupus that the internal factors are not able to render the skin capable of eliminating or terminating the tuberculous

process. Hence it seems important that the term tuberculid be retained, in contrast always to lupus vulgaris.

What is the pathogenesis of the tuberculids? The most likely explanation is that the organisms are brought to the parts through the blood stream. Why the bacilli lodge in certain areas, especially the face, and produce lesions there cannot be explained. Why one particular type of lesion develops instead of another, of course, cannot be explained either. If it were known why lesions of tuberculosis develop in certain areas and what predisposes the tissues to a certain kind of response, it would be possible to predict events in cases of tuberculosis of the skin, which is now impossible. Immunologic studies have not yet afforded

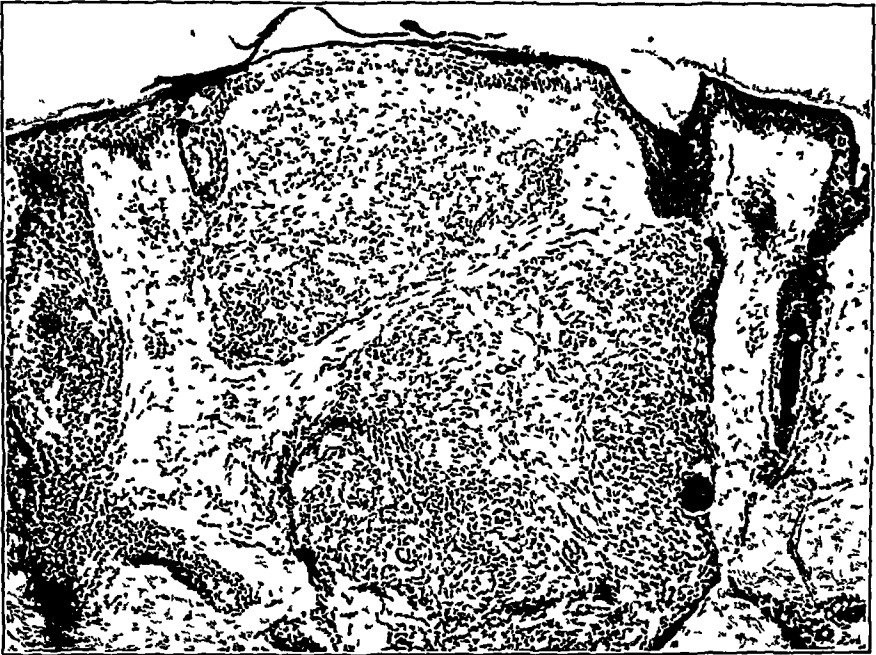


Fig 3—Histologic structure in case 2 (fig 2). There were nodules of infiltrate in the upper and middle parts of the cutis. The structure simulated that of sarcoid, being composed chiefly of epithelioid cells. There were a few giant cells and lymphocytes.

an answer to the question. The studies of Jadassohn and his pupils have shown that quantitative intradermal tuberculin tests elicit reactions which are different in patients with tuberculoderms from those observed in normal persons. The sarcoid group is well known for its hyposen-sitivity to tuberculin. We do not believe that one can say that a par-ticular degree of hypersensitivity to tuberculin must accompany a certain type of tuberculous lesion in order to make the diagnosis tenable.

Observation over many years has established well known facts about such forms of tuberculosis as lupus vulgaris, acnitis and lupus miliaris

disseminatus faciei. Additional information and opinion concerning a less well known type, such as the micropapular tuberculid, should be recorded, so that as much as possible may be learned about it.

We may begin the classification, then, with this smallest type of tuberculid, the micropapular.

A case of this kind was presented at a meeting of the Dermatologic Reunion of Strasbourg on Nov. 21, 1937 by Pautrier and Lanzenberg,^{1a}

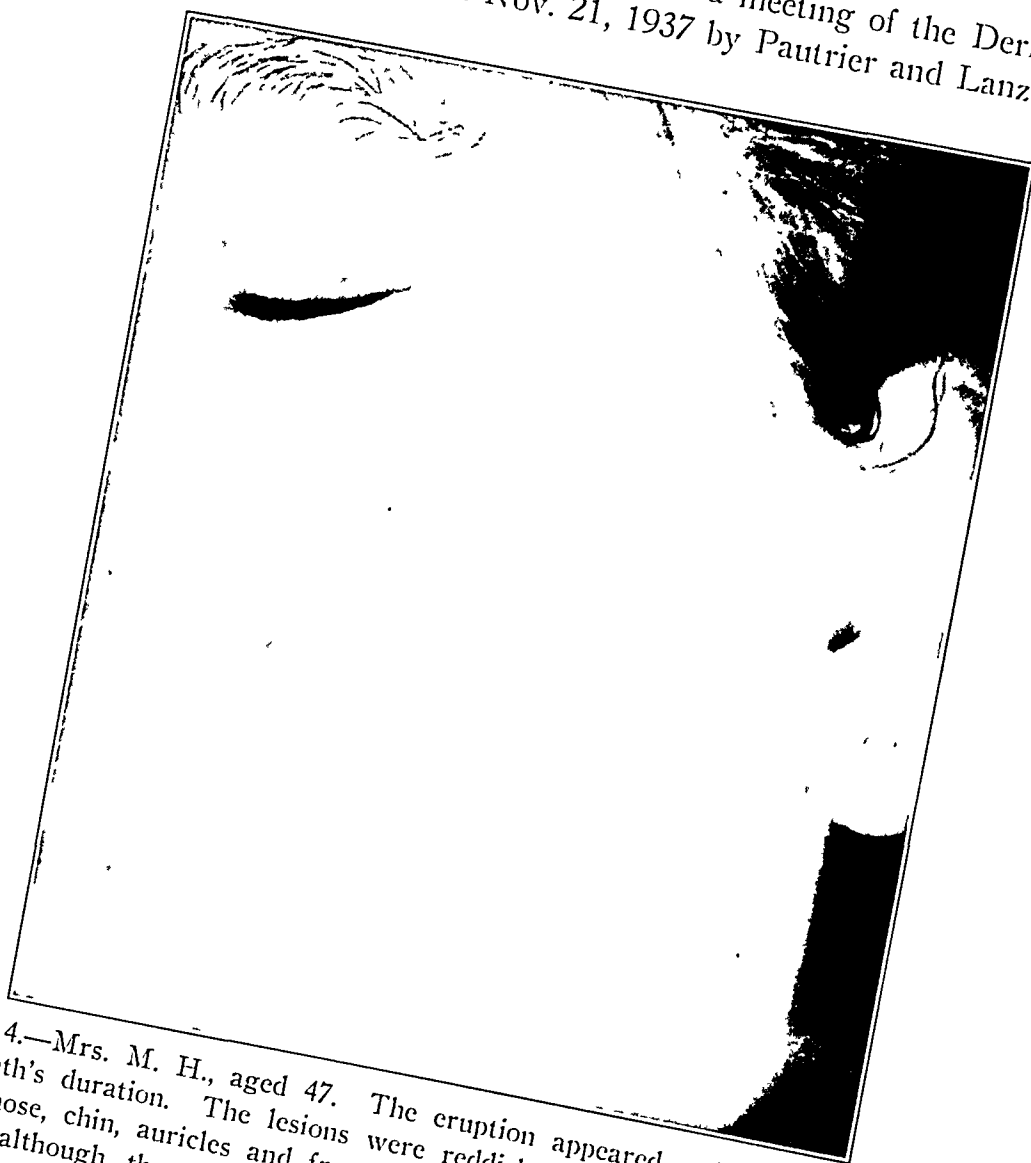


Fig. 4.—Mrs. M. H., aged 47. The eruption appeared suddenly and was of one month's duration. The lesions were reddish brown papules situated on the cheeks, nose, chin, auricles and front of the neck. There was a resemblance to rosacea, although there were no pustules. The Mantoux reaction (1:1,000) was strongly positive. There was no clinical evidence of pulmonary tuberculosis. Response to treatment (roentgen irradiation and administration of gold sodium thiosulfate) was slow. There was great improvement, but not complete involution, within four months. The subsequent history is not known.

Under the title of "micronodular tuberculid." Since then, at subsequent meetings⁵ of the same society, 3 additional cases have been described.

5. Pautrier and Woringier.^{4b} Pautrier.^{4c} Pautrier and Woringier.^{4d}

In Pautrier's cases the lesions, which appeared suddenly on the face, consisted of small, round, raised brownish violet papules which were distributed over the forehead, nose, cheeks and chin. In 1 the ears were involved, and in another there were papules on the neck and chest. The individual lesions were sharply circumscribed and showed a yellowish brown stain on application of diascopic pressure. Necrosis and ulceration were entirely absent.

In all of the 4 cases described by Pautrier the cutaneous reactions to tuberculin in dilutions of 1:1,000 were positive. No active focus of internal tuberculosis was discovered in any of the 4 cases, although 1 patient presented roentgen signs of old healed pulmonary tuberculosis.

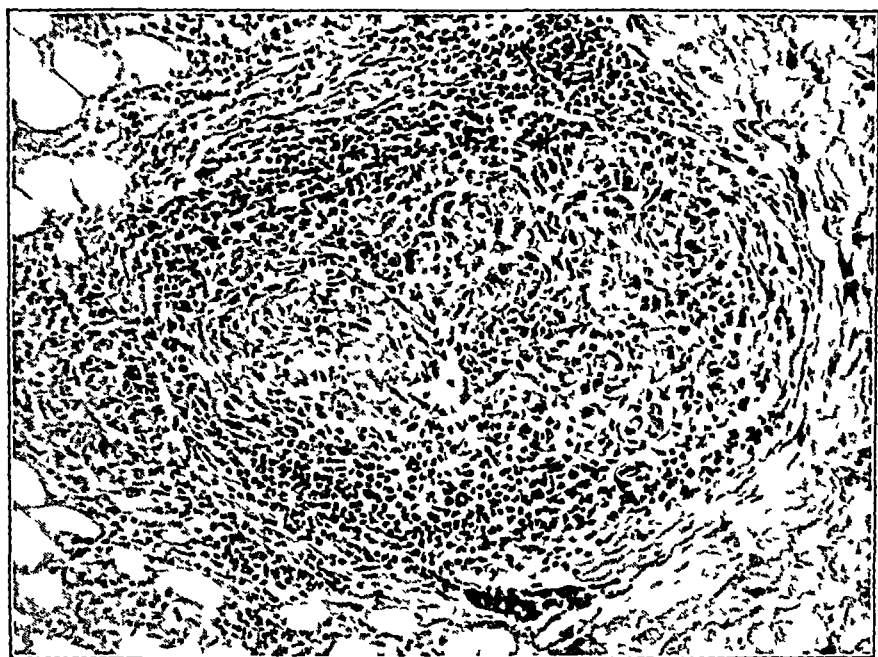


Fig. 5—Histologic structure in the case illustrated by figure 4. The tuberculoid structure was deep in the cutis.

The 14 patients whom we have observed presented similar eruptions, occurring predominantly on the face, although in a few cases papules were present on the neck. The lesions differed from those of acutis in that they were smaller, more numerous, not elevated and without macroscopic central necrosis. After disappearance of the lesions, varioliform scars often resulted. In some cases the eruption consisted entirely of these small papules, while in others there were papules and some hyperemia, which somewhat suggested rosacea. The basic papules appeared to be localized in the skin and not on the surface. The course of the disease was prolonged into months or even years but under management often came under control, and no new lesions formed.

When the lesions underwent involution they did so altogether in contrast to those of lupus miliaris disseminatus faciei, which disappear a few at a time. A history of actual tuberculosis or close association with tuberculous relatives could be elicited in most cases. The reactions to tuberculin (Mantoux 1:1,000) were positive in 12 of our cases and negative in 2. In the latter group it was extremely difficult to differentiate between micropapular tuberculid and sarcoid on the basis of



Fig. 6.—Mrs. L. A. C., aged 55. The duration of the eruption was one year. It was confined to the face.

either the clinical or the histologic observations. The relatively short course, however, led us to classify the lesions as the micropapular tuberculid.

In histologic sections Pautrier observed an infiltrate which was tuberculoid in structure and was located especially about the follicles. There was a tendency to disintegration of the tissues in the involved areas. For the most part the pathologic process appeared well circumscribed and sharply demarcated from the surrounding tissues. About the areas

of necrosis were numerous polymorphonuclear leukocytes forming tiny abscesses. At the periphery of such areas a heavy infiltrate was noted, consisting of lymphocytes, epithelioid cells and numerous giant cells. In certain places the capillaries were dilated and engorged with red blood cells. The epidermis overlying the lesions remained intact.

Pautrier and Woringer stated the belief that the histologic character of the micropapular tuberculid can be closely aligned with that of the



Fig 7—Histologic structure in the case illustrated by figure 6. There was an epithelioid type of tuberculoid structure extending throughout the cutis.

papulonecrotic tuberculid. In the former, however, the areas of necrosis are less extensive and do not encroach on or disrupt the continuity of the epidermis. In Pautrier and Woringer's opinion there are also rather intimate resemblances to lupus miliaris disseminatus faciei, the tuberculoid mass in the latter, however, is much more inflammatory and accompanied by more edema. Pautrier and Woringer stated that the central necrosis in lupus miliaris disseminatus faciei is less pronounced and more fibrinoid in appearance. The authors expressed the opinion

that it is difficult to separate these tuberculoderms on a purely histologic basis and that they are morphogenetically the same.

In order to evaluate the histologic observations associated with the micropapular tuberculid we thought it advisable to perform biopsies of the lesions of patients with incontestable rosacea. Accordingly, we examined sections from 30 such patients, and we believe that there should be no confusion microscopically between true rosacea and the tuberculids of the face. In those cases of rosacea in which giant cells are observed, they are usually located about a destroyed follicle, and true tubercle formation or even collections of epithelioid cells are absent.

We examined many sections from the 14 patients who had what we have critically diagnosed as micropapular tuberculid. In all instances in which there was any confusion concerning another form of tubercu-

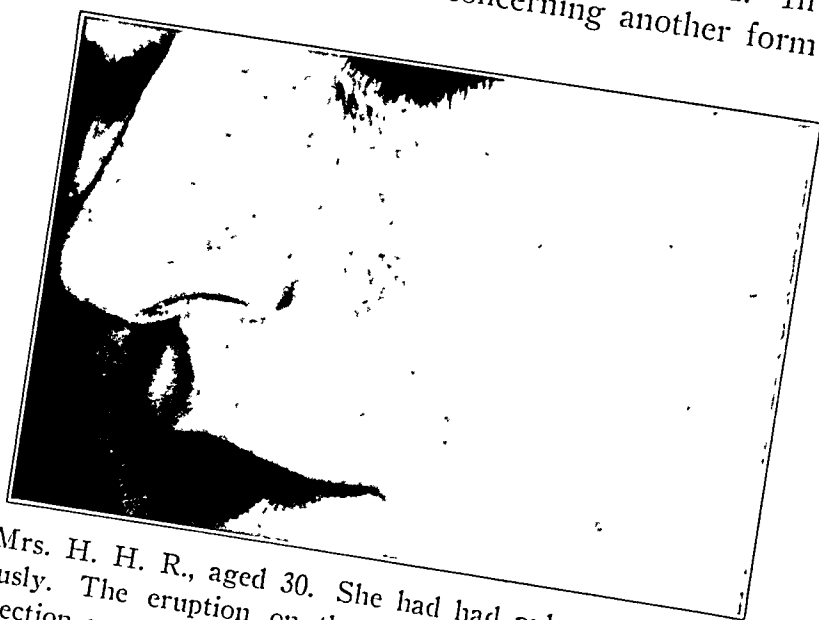


Fig. 8.—Mrs. H. H. R., aged 30. She had had pulmonary tuberculosis twelve years previously. The eruption on the face was of two years duration. The microscopic section revealed a tuberculoid structure.

losis we excluded the sections from this analysis. We were immediately impressed by the fact that a pathognomonic picture was lacking, and we realized that even though our clinical diagnosis seemed certain beyond a shadow of a doubt we could never anticipate what the histologic picture would be.

The chief impression which we gained from a survey of our sections was that the micronodular tuberculid can be aligned histologically with the chronic indurative type of tuberculosis. In analyzing the component parts of the skin from these patients we found that the epidermis was almost invariably atrophic, which is in keeping with the observations in cases of lupus miliaris disseminatus faciei and sarcoid but in distinct contrast to those associated with lupus vulgaris, with which acanthosis

is often noted. The epidermis also remained intact, which is in contradistinction to the papulonecrotic tuberculid.

As was to be expected, the infiltrate varied in every case. In some sections it was high in the corium and consisted of whorls of pure epithelioid cells with an occasional giant cell and no coexisting acute inflammation. In other sections the infiltrate appeared as vertically placed lobes extending down to the hypoderm. Still another type of



Fig 9—Mrs F C, aged 36. The eruption was of three years' duration. The Mantoux reaction (1:1,000) was positive. There were no signs of visceral tuberculosis.

infiltrate noted was tuberculoid structure surrounded by considerable banal inflammation. Necrosis and liquefaction were not encountered.

In summarizing the histologic picture of the micropapular tuberculid we wish to stress its extreme similarity to that of sarcoid. Had we not studied the eruption clinically we should have made a diagnosis of sarcoid from some of the sections alone. For comparison we also studied tissues from 8 patients with unquestionable sarcoid on the face and 5 patients with lupus miliaris disseminatus faciei. We found it difficult to draw

sharp lines of differentiation between any two of the three conditions, and we are certain that histologic examination alone is inadequate for an accurate diagnosis.

If one considers the course of the tuberculids, lupus vulgaris, cutaneous sarcoids and tuberculosis colliquativa, one is impressed by the fact that the tuberculids require the shortest time to complete their cycle, being followed by the sarcoids, tuberculosis colliquativa and lupus vulgaris respectively. In attempting to classify a form like the micropapular tuberculoderm it is important that one associate it with the tuberculids because of its sudden appearance and its healing within a relatively short period.

Pautrier expressed the belief that the micropapular tuberculid is closely related to acnitis and that the latter represents basically the micropapular tuberculid in which the pathologic changes are more severe and destructive, leading to clinically demonstrable necrosis. Evidently his examinations led him to this conclusion, while from our own studies we are inclined to align the condition with the lupoid types. Also, the dividing line between the micropapular tuberculid and lupus miliaris disseminatus faciei is certainly not sharp, the chief difference being that the lesions of the latter are larger and fewer. In all probability many cases of micropapular tuberculid have been demonstrated as examples of lupus miliaris disseminatus faciei.

Continuing the classification based on variations in the size and type of papule in the various tuberculids, we should like to propose the term "lupoid papular tuberculid" for lupus miliaris disseminatus faciei.

For many years authorities have been perplexed in classifying this form, and there has been much debate as to whether it should be grouped with true lupus vulgaris or with the tuberculids. If one recalls the criteria which were previously outlined for the tuberculids, one is at once driven to group this type with the tuberculids, since it fulfils all the criteria, even though an individual lesion may be indistinguishable from a single nodule of lupus vulgaris or a papule of sarcoid. The lupoid papular tuberculid (lupus miliaris disseminatus faciei) may, then, be the transitional condition between the relatively fixed tuberculoderms, such as lupus vulgaris on the one hand and the more labile tuberculids on the other.

Well developed lupoid papular tuberculids are characterized by firm, discrete papules which occur singly or in groups and vary in color from light pink to brownish red. The eruption is confined to the face and is often seen about the eyelids, cheeks and mucocutaneous surfaces of the lips. Even the neck is unaffected. The individual lesions cannot be differentiated from minute nodules of lupus vulgaris. As a rule, however, those of the lupoid papular type are harder, do not enlarge by continuity and remain discrete throughout their course. The papules

attain their maximum size and number shortly after their appearance and remain stationary throughout the long course of the disease. There is no reaction of the skin surrounding the lesions as in the necrotic papular tuberculid. Edema, suppuration or change in the contour of the face is lacking. With a probe or a microcautery one can pass readily through the tuberculous infiltrate and feel the resistance of the harder surrounding tissues. Healing is spontaneous, the lesions gradually shrinking away without sloughing or crusting and leaving small pitted scars.

In our examinations we have found that the histologic changes are inconstant. This is in contrast to the opinion, almost universally expressed in the literature, that this type of tuberculid has a well defined microscopic picture. This picture depends to some extent on the time in the course of the disease when the excision was made and the precise location of the section. We have found well demarcated, globular masses of tuberculoid infiltrate made up of epithelioid cells, giant cells and lymphocytes, which were located high in the corium. Although necrosis is not a clinical feature, central caseation was seen in some sections, surrounded by an inflammatory mass separating it from the surrounding tissues. Tubercle bacilli have been demonstrated in such sections. Patients who have the lupoid papular tuberculid are usually hypersensitive to tuberculin. Some observers, however, have noted the opposite.

In the classic form of lupoid papular tuberculid the strict localization to the face should again be emphasized, because in this respect this condition stands in sharp contrast to acnitis and milium sarcoid. Another point which has impressed itself on our minds is that patients who have had the lupoid papular tuberculid and who have been followed for many years have never reported a recurrence, which is quite different from our experience with the necrotic papular tuberculid.

The necrotic papular tuberculid constitutes the third main subdivision of the tuberculids. In our opinion the term necrotic papular tuberculid is preferable to such designations as acnitis, folliculitis and papulonecrotic tuberculid, since it again emphasizes the papule as the basic lesion. As a rule, this type of tuberculid is not confined to the face, which is usually involved as part of a more or less general outbreak. This may be significant, in that the entire organism is in a higher state of response to the invading organism. Necrotic papular tuberculids are shotty papules which stand above the level of the surrounding skin and often have central necrosis, which may be destructive, giving rise to scars when healing occurs. The lesions are dark red or bluish red rather than the brownish red or apple jelly color of the papules in the lupoid papular tuberculid. The lesions develop rapidly, are extremely labile and accordingly run a short course and disappear, resembling a suppurating folliculitis or small furuncles. The time between attacks is variable, it

may be years, or a new series of lesions may appear as the earlier ones are healing. A more or less continuous appearance and disappearance of sparse but widely disseminated papules has also been noted. We have often seen necrotic papular lesions side by side with the deeper plaques of erythema induratum, and we believe that they are essentially the same lesions, varying only in size and depth.

Histologically the necrotic papular tuberculid is characterized by a central area of acute necrosis surrounded by a zone of inflammation which may be tuberculoid in structure, especially at the periphery. The histologic observations are uniform in type but not in extent. There is no need to enlarge further on the histologic features, which are well known.

Patients having the necrotic papular tuberculid react strongly to tuberculin. Internal tuberculousis can almost always be found in these patients.

Many astute observers have pondered over the specificity of the necrotic papular lesion and its wide extent. Its coexistence with other follicular lesions, including acne vulgaris, again leads us to hypothesize that this type of person has a tendency to develop acneiform lesions.

The small papular varieties of sarcoid, especially on the face, may easily be confused with the micropapular or lupoid papular tuberculid. The papules of sarcoid on the face are harder, and necrosis and ulceration are entirely lacking. Their color is usually pink or light reddish brown, and frequently they exhibit a peculiar opalescence or translucence. The development is gradual; the course is slower than that of any of the other conditions under consideration, and regression is much delayed. In contrast to the lupoid papular tuberculid, new lesions frequently develop while the papules of sarcoid always remains intact. There may be considerable erythema of the skin, resembling rosacea. There is regression of the lesions of sarcoid always remains intact. There is even telangiectatic, but varioliform scarring does not result as in the other conditions under discussion.

Histologically the lesions may be made up entirely of closely packed epithelioid cells divided by septums of connective tissue. At times giant cells are present in varying numbers, and an encircling wall of lymphocytes is occasionally observed. Necrosis and ulceration are never encountered.

The extreme chronicity of cutaneous sarcoids, the lack of subjective symptoms and the absence of ulceration, coupled with characteristic histopathologic observations and hyposensitivity to tuberculin, are the chief points in differential diagnosis. Lesions in other organs are frequently encountered.

In this presentation it has not been our intent to offer a new nomenclature but to set forth our views on the tuberculids of the face and to make suggestions toward a simpler terminology founded on variations in the size and type of the essential lesion of all tuberculids, the papule. Following this concept, we believe that the designation micropapular tuberculid is an apt one for a basic type of tuberculid which in certain patients bears a striking resemblance to rosacea.

In the difficulty encountered in properly diagnosing tuberculids of the face one should take many factors into consideration. Undue emphasis should not be placed on the distribution alone, nor should an impression be gained from the initial inspection of the eruption, since repeated observations are frequently necessary for accurate diagnosis.

A definite decision having been made that the case is one of tuberculosis, the next step is to rule out lupus vulgaris and sarcoid, a procedure which for the latter condition may be extremely difficult, since the small papular varieties closely resemble facial tuberculids both clinically and histologically. If this has been accomplished, the decision will be between the three main types of tuberculids, the micropapular, the lupoid papular and the necrotic papular.

The features of the eruption, such as the size, color, shape, age, number of the lesions and presence or absence of secondary changes, such as pustules and hyperemia, are the chief factors in arriving at a diagnosis. It should again be emphasized that the histologic observations are, as a rule, not conclusive. In eruptions resembling rosacea we have found that the histologic structure was definitely that of sarcoid. We have also been impressed with the fact that in certain cases which clinically were classic examples of the lupoid papular tuberculid the histologic picture strikingly simulated that of sarcoid. Thus a careful analysis of all the factors of a facial tuberculoderm is essential to accurate diagnosis, and the latter is a requisite for correct prognosis.

In studies of cutaneous tuberculosis, unfortunately, the diagnosis is often made without demonstration of the tubercle bacillus, for this is a tedious and often unfruitful procedure. Since there is no serologic test for tuberculosis, there is a certain presumption in classifying what we have called micropapular tuberculid with tuberculosis. This, however, also applies to sarcoid, and one must constantly keep in mind that the future may reveal other causes for these conditions.

In attempting to take a kaleidoscopic view of this condition one sees on the one extreme the patient with the diffusely erythematous eruption closely simulating mild so-called lupus pernio and on the other extreme the patient presenting multiple closely studded papules involving almost the entire face. Between the extremes will be found the average for this condition, that is, an eruption consisting of small papules as previously described. In our opinion the term micropapular is preferable to rosacea-like tuberculid.

ABSTRACT OF DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Drs. Laymon and Michelson have given a very clear presentation. It is true that there are micropapular or micronodular tuberculids of the face which do not show features of the rosacea-like tuberculid of Lewandowsky or of lupus miliaris disseminatus. Where should one draw the distinction between the papule and the nodule? Histologically, in the cases presented by Drs. Laymon and Michelson the lesions extended down to the hair follicles, and in other cases I have seen them extending even into the subcutaneous tissues. Therefore, histologically one is dealing with minute nodules and not papules. Clinically and histologically, so-called papulonecrotic tuberculid is definitely a nodular and not a papular eruption.

Although the term "rosacea-like tuberculid" may be somewhat confusing to students, I should not like to see it abandoned, because in many cases micropapular or micronodular tuberculid has features of rosacea, and it is frequently misdiagnosed as acne rosacea. All transitions between lupus miliaris disseminatus and rosacea-like tuberculid may be seen, and all represent hematogenous forms of tuberculosis. This is also true of sarcoids, including the so-called miliary types. It is my belief that there are too many subdivisions of cutaneous tuberculosis based purely on morphologic grounds. Thus, the sarcoid of Boeck is superficial; the sarcoid of Darier-Roussy is simply a deep subcutaneous form of sarcoid, and lupus pernio histologically is sarcoid of Boeck plus superficial dilatation of the capillaries and lymphatics. All are hematogenous types of tuberculosis.

Much remains to be explained in regard to cutaneous types of tuberculosis. For instance, in lupus miliaris disseminatus (tuberculosis cutis follicularis disseminatus) the tuberculin reaction is usually negative, yet the histologic picture is characteristically that of tuberculosis, showing many typical tubercles and definite caseation necrosis, whereas many of the rosacea-like tuberculids, including the papular or nodular type just described by the authors, may coexist with a positive tuberculin reaction and histologically show small epithelioid tubercles simulating the pathologic picture seen in various types of sarcoid.

DR. CLARK W. FINNERUD, Chicago: I should like to ask Dr. Laymon where in this classification he would include acne telangiectodes of Kaposi. In my opinion, and I saw a goodly number of cases of this condition in Vienna, it does not fit in clinically with acnitis, with the so-called rosacea-like tuberculid of Lewandowsky or with lupus miliaris disseminatus faciei.

DR. JAMES R. DRIVER, Cleveland: What I have to say is not particularly on the subject, as treatment has not been spoken of, but I should like to record an experience that I had recently with a case of lupus miliaris of this lupoid papular type in a patient who had about twenty lesions on the face. I used solid carbon dioxide, and a single treatment to each of the lesions made them disappear. To date there has been no recurrence.

DR. HENRY E. MICHELSON, Minneapolis: Dr. Laymon and I well realize that, when tuberculosis is the subject for discussion, a great deal can be said and that we could probably not convince any one whose views are fixed that our viewpoint is the correct one. However, we have no such intention. We thought that the term "rosacea-like tuberculid" had been used too freely, and when we attended clinical meetings we saw patients whose condition was so labeled but that did not give us, at least, the impression of tuberculosis. At best, the diagnosis of rosacea-like tuberculid is not an easy one, and possibly such an entity exists and cannot be definitely alined with tuberculosis. To me it is a great deal like seeing

a horse with a long neck and calling it a giraffe-like horse. It is still a horse. If this condition is tuberculosis the nomenclature should be based on that conception alone.

Dr. Montgomery has given such a broad survey of the whole subject of cutaneous tuberculosis that I shall not attempt to answer any particular part of his discussion. I do not know just where the line between a papule and a nodule is. One always thinks of a nodule as a larger lesion than a papule, and because the lesions in this particular type of disease are so small, we call them micro-papules. The lupoid papular tuberculid, the so-called military facial lupus, is not follicular, that we are convinced of. The article of Arndt proved this long ago, and we have verified his work repeatedly.

I should like to call your attention to the fact that there may be many bacilli of tuberculosis in the skin of tuberculous persons which do not produce lesions. Keeping this in mind, Dr. E. M. Rusten and I are making excisions from patients at the Glen Lake Sanatorium to determine whether tuberculoid structure is present in banal conditions in the tuberculous patient.

The tuberculin test has been overrated, to my mind, as an aid in the differential diagnosis of different forms of cutaneous tuberculosis. About treatment, it is my feeling that in most patients with the type of facial tuberculosis that we are discussing the condition takes a course which is fairly individual for each patient. Some get well rapidly and others much more slowly. We have not observed recurrences, but possibly time will cause us to change that statement.

ARSENIC AS THE CAUSE OF CANCER OF MUCOUS MEMBRANE

REPORT OF A CASE

W. H. GOECKERMAN, M.D.
AND

L. F. X. WILHELM, M.D.
LOS ANGELES

Arsenic in its inorganic form is now fully accepted as a cancerigenic agent. Whether this is also true of the organic forms is still doubtful; although malignant changes probably follow their administration, the changes may be the result of arsenic as an element. If so, it would seem to work its havoc as the result of chronic irritation rather than of any specific cancerigenic qualities, and the common cutaneous lesions produced ever. In the case reported here the case was of unusual interest because it by arsenic were present but the case was of unusual interest because it was possible to demonstrate the metal in a papilloma and a carcinoma of the internal mucous membranes by microchemical studies, thus proving beyond much doubt that arsenic was at least a factor.

REPORT OF CASE

The patient, a retired physician now aged 70 years, was first seen by us in 1928. At that time he complained of keratotic lesions of the palms and soles and of large numbers of erythematous, scaling plaques, some indurated and some ulcerating, on the trunk, thighs and legs (fig. 1). The familial and the early personal history were not relevant. Epilepsy developed in 1904, when he was 34 years old. Dr. Hugh Patrick at that time prescribed solution of potassium arsenite U. S. P. (Fowler's solution), which the patient took steadily until 1914, when he changed to sodium phenobarbital and took no more arsenic. At one time Dr. Harvey Cushing performed an exploratory operation in the right temporoparietal region but found no abnormalities. There was no history of venereal disease, and repeated Wassermann tests of the blood gave negative reactions. He first noticed the palmar and plantar keratosis in 1918, four years after he had stopped taking arsenic, and the first lesions appeared on the trunk a year or two later.

Examination showed him to be healthy looking, with no internal complaints; the problem that concerned him when first seen was that of the cutaneous lesions, particularly the tendency of some of them to ulcerate. These all healed, however, after treatment with roentgen rays or destructive measures whenever treatment was thought desirable.

Read at the Sixty-third Annual Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., May 31, 1940.

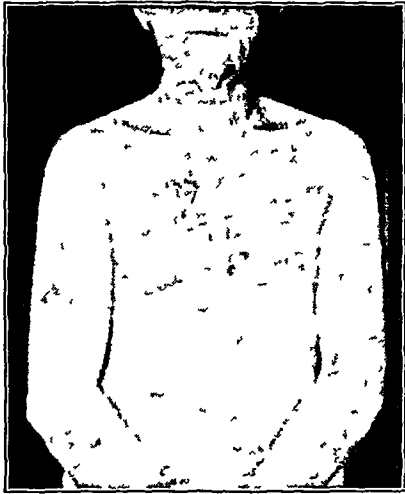


Fig 1—Arsenical keratoses on the chest, arms and abdomen



Fig 2—Basal cell epithelioma in arsenical keratosis × 85

In July 1935, for the first time, he noticed in the voided urine a brownish discoloration, some blood clots and pus. Occasionally he also noticed slight suprapubic aching and slowing of the urinary stream. He was then referred to a urologist, who in August removed the right ureter and kidney. The lower third of the ureter contained a soft, movable mass about 15 cm. in its greatest diameter, which on microscopic examination was pronounced a papilloma. After the operation there was an uneventful recovery, but in December of the same year he again complained of symptoms referable to the urinary tract. Cystoscopic examination

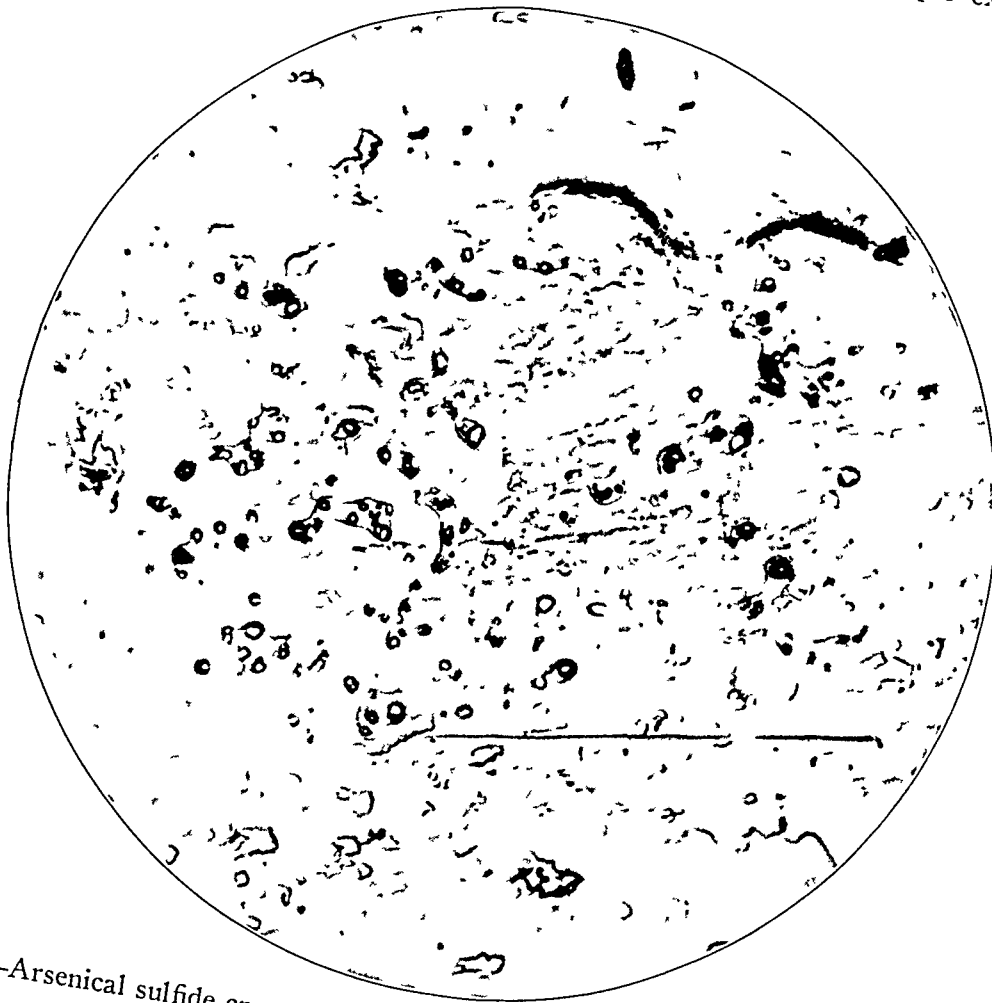


Fig. 3.—Arsenical sulfide crystals in a section stained by Osborne's method. $\times 600$.

showed papillomatous lesions behind the vesical neck and posteriorly. These growths were subjected to biopsy and fulgurated transurethrally. The pathologist reported them as malignant. A second fulguration was performed in 1936. Since then the patient has had no complaints except those referable to the skin.

Pathologic Studies.—Microscopic examination of the ureteral papilloma showed a definite papillomatous structure. The epithelial cells stained deeply; they were irregular in size and shape, with pyknotic nuclei. Mitotic figures were rare. There was considerable round cell and eosinophilic infiltration. There was no definite evidence of malignancy, but the urologic literature indicates that all ureteral papillomas in the course of time become malignant.

Microscopic examination of the papillomatous growths of the bladder showed definite malignant changes. A section recently removed from an area of chronic dermatitis without evidence of ulceration did not show anything to point to malignant changes. Another section, subsequently removed, macroscopically strongly suggested Bowen's disease but microscopically was a rather typical basal cell epithelioma (fig 2). Sections of the papilloma of the ureter, the malignant tumor of the bladder and the skin were studied by Osborne's method. The vesical carcinoma showed many arsenic crystals (fig 3), but only occasional crystals were seen in the ureteral papilloma and in the first section of skin. The second section of skin was not subjected to microchemical study.

COMMENT

The patient presented classic arsenical keratoses of the palms and soles. The keratoses of the trunk and extremities were of the arsenical rather than of the superficial epitheliomatosis type, if strict differentiation is justifiable. Some of the keratoses strongly suggested Bowen's disease, one such lesion being examined microscopically. A section of a simple keratotic lesion of the trunk merely showed dermatitis and the presence of arsenic crystals in moderate amount, which, as Montgomery has recently emphasized, is not necessarily of etiologic significance. Of particular interest was the development of a ureteral papilloma, potentially malignant, and of definitely malignant vesical papillomas in a patient with a prolonged history of ingestion of arsenic. In the ureteral papilloma arsenic was demonstrated in a moderate amount and in the vesical papillomas in a considerable amount. While it is true that the mere presence of arsenic in a lesion does not incriminate this element as the etiologic factor, we feel that the evidence is about as good as can be obtained today that arsenic was at least a factor in the production of this patient's ureteral and vesical papillomas, admitting freely the existence of an undiscovered etiologic factor or factors in all cancer.

LITERATURE

Since in the case reported the evidence points strongly to arsenic as a causative factor not only of precancerous cutaneous lesions but of precancerous and evidently cancerous lesions of the mucous membranes, the thought arises that arsenic may frequently be the cause of cancer in certain areas, such as the gastrointestinal, the respiratory and the genito-urinary tract. This question manifestly has not been given the attention it deserves. All modern studies indicate that arsenic is introduced into the human body as the result of a variety of factors, such as ingestion of sprayed vegetables and fruits, drinking of contaminated water, inhalation of dust containing arsenic used in horticulture and agriculture, exposure in mines or in industry and administration of arsenic as a medicament. In contrast to a large number of studies indicating the almost universal

presence of arsenic in the human body, it is impossible to find any studies of the presence of arsenic in a series of carcinomas of the mucous membranes. It might be assumed that if arsenic were a reasonably frequent cause of such lesions the arsenic eaters in Styria might be a fertile field for investigation. The literature strongly indicates, however, that the whole story of these arsenic eaters is largely a myth.

Two large groups exposed for considerable periods and to quantities of arsenic are arsenic miners and persons employed in the sheep dip industry, but even among these there is, so far as the literature is concerned, no evidence that arsenic is a common cause of cancer of the mucous membranes. However, there is also no evidence that such carcinomas as occur have been studied by microchemical methods. The one exception is pulmonary cancer as seen in arsenic miners, but in this condition arsenic probably acts as a direct irritant to the lining of the trachea and bronchial tree. It was difficult to find any concrete cases reported in which arsenic was probably the cause of cancer of mucous membrane as the result of hematogenous distribution. Ullmann¹ cited the case of a woman who had taken solution of potassium arsenite (Fowler's solution) for years; the common cutaneous complications developed, and toward the end there occurred cancer of the tongue and of only 4 cases of cancer of the mucous membranes, 1 each of lingual, oral, anal and vulvar carcinoma. If these were individually reported, we had no access to the reports. Morson,³ although he did not specifically make this claim for arsenic, rather emphatically expressed the belief that dyes and other chemicals through hematogenous distribution may be the cause of cancer of the genitourinary tract. It would seem either that arsenic is rarely the cause of cancer of the mucous membranes through hematogenous distribution or that the whole problem has not received the investigation it deserves. In our opinion a series of carcinomas of the mucous membranes, e. g., those of the stomach, should be examined by microchemical methods even when the patient has no other evidence of injury due to arsenic. While we are fully aware that the mere demonstration of arsenic sulfide crystals in a carcinoma does not prove that arsenic has been an etiologic agent, such a demonstration in a series of carcinomas would point to arsenic as a possible factor. It is an accepted fact that arsenic does not affect all persons in the same manner; hence some have keratoses after small medicinal doses, and others do not, even

1. Ullmann, K., in Jadassohn, J.: *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1932, vol. 12, pt. 2, p. 619.
2. Mayer, R. L., in Jadassohn, J.: *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1933, vol. 4, pt. 2, p. 64.
3. Morson, C.: *Brit. J. Urol.* **5**:333, 1933.

after prolonged use Mayer⁴ emphasized the experimental fact that a 1 40,000,000 solution of arsenic will change embryonal cells to tumor cells. Some keratoses become cancerous and others do not, even in the same person. It does not seem unreasonable, therefore, to assume that cancers of mucous membrane may develop as the result of hematogenous distribution of arsenic without the presence of the well known cutaneous lesions.

SUMMARY

A case is reported in which cutaneous eruptions due to arsenic were followed by cancer of the mucous membranes of the ureter and bladder. Arsenic was demonstrated by microchemical methods in all the growths but in largest quantity in the cancer of the bladder. This, so far as we could learn, is the only case of this kind so far reported.

It would seem that either cancer of the mucous membranes due to hematogenous distribution of arsenic is very rare or the matter has not been sufficiently investigated.

Drs. Rusche and Bacon have furnished sections of the ureteral papilloma and the vesical carcinoma for further study. Dr. Hamilton Montgomery's opinion was obtained on these sections as well as on the first section taken from the skin.

ABSTRACT OF DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester, Minn. This subject has been of great interest to me. I might cite case 2 in a former report of my own (Arsenic as an Eitologic Agent in Certain Types of Epithelioma, *ARCH. DERMAT. & SYPH.* **32** 218-236 [Aug.] 1935). A farmer aged 42 years was first seen in the clinic in 1927. He had epithelioma of the left sole following arsenical keratoses. The lesion histologically was a squamous cell epithelioma, grade 3. Seven years later there developed numerous arsenical epitheliomas on the trunk, histologically grade 1 and 2 squamous cell epitheliomas, and one superficial epithelioma, histologically a basal cell epithelioma. Crystals of arsenic trisulfide were demonstrated in the epithelioma of the arsenical type. In February 1934 there developed an intra-urethral epithelioma, grade 3, also arsenical. The penis was partially amputated. There had been no recurrence of the intraurethral epithelioma when the patient was seen in 1938, at which time a bronchoscopic examination revealed a grade 4 epithelioma of the bronchus. Again this tumor showed vacuolation of cells and malignant dyskeratosis simulating Bowen's disease, which is a characteristic feature of the arsenical type of epithelioma. The patient died of extensive metastases in February 1940.

I have pointed out that it is important to distinguish between superficial epitheliomatosis, Bowen's disease and superficial epitheliomas arising from arsenical keratoses or as a result of ingestion of arsenic independent of the keratoses (Precancerous Dermatoses and Epithelioma in Situ, *ARCH. DERMAT. & SYPH.* **39** 387-408 [March] 1939). In 4 cases of superficial epitheliomatosis that I have studied recently the growths had fine threadlike borders and histologically were typical

⁴ Mayer, R. L., in Jadassohn, J. *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1933, vol. 4, pt. 2, p. 72.

basal cell epitheliomas but revealed no arsenic either by quantitative chemical analysis or by the microchemical method of Osborne. Osborne's method I believe to be accurate if used with fresh formaldehyde-fixed tissue and with proper technic. The case reported by Drs. Goeckerman and Wilhelm and the subsequent course in the case which I previously reported emphasize that the mucous membranes are not infrequently involved in cases of the arsenical type of epithelioma.

DR. NELSON PAUL ANDERSON, Los Angeles: Drs. Goeckerman and Wilhelm are to be complimented on producing the first paper in the English language calling attention to the possible role of arsenic as a carcinogenic agent in cancer of the mucous membrane.

As they more or less limited their paper to that phase of the subject, I shall not discuss the cutaneous manifestations of arsenic intoxication in which I have been interested for some time.

Recently I have seen a man about 21 years of age who at the age of 14 took arsenic for about six months. At 21 years of age he presented multiple arsenical keratoses on the palms and soles, multiple superficial epitheliomas of the trunk, a large fungating grade 2 prickle cell epithelioma in one groin and an extremely large fungating carcinoma of the tongue. It is suggestive that all of these lesions were present at one time.

I think all dermatologists will admit that keratoses of the palms and soles of a certain type are due only to arsenic. Some believe that most of the superficial epitheliomas of the trunk are due to arsenic. When, in addition, there are prickle cell epitheliomas on the cutaneous surface and a prickle cell epithelioma of the tongue, I think the conclusion may be drawn from clinical grounds alone that arsenic is undoubtedly a factor in producing cancer of the mucous membranes.

I think that as time goes on further observations will be made which will bear out this original piece of work indicating that arsenic is not to be neglected as an etiologic agent in any mucous membrane carcinoma.

DR. LOUIS SCHWARTZ, Washington, D. C.: I thank you for granting me the privilege of making a few remarks.

I have heard papers presented on arsenical keratoses a number of times, and I have also seen arsenical keratoses. In every case the arsenical keratoses were caused by ingestion of arsenic and never by contact with arsenic.

Many of the European writers, for example, Prosser-White and Oppenheim, have mentioned that arsenical keratoses and arsenical carcinomas occur in miners having contact with arsenic-containing ores.

The public health service made a survey of cutaneous hazards among workers handling arsenic in the United States. During the course of this survey hundreds of men who manufacture arsenical insecticides and thousands of men who use arsenical insecticides in orchards in California, Florida and other states were examined. No case of arsenical keratoses or arsenical cancer was observed among these men, whose skins and, perhaps, lungs are exposed to arsenical dusts.

Moreover, in studying the records of compensation boards for the last six years—that is, compensation boards for industrial diseases—that come to the office (in all the states which have compensation boards cases are reported to the public health service) no case of arsenical cancer among industrial workers has been encountered.

This brings out the fact that arsenical keratoses and arsenical cancers are apparently caused by ingestion of arsenic through the intestinal tract or by intravenous injection of arsenic, and not by contact of the skin with the drug.

DR GEORGE C ANDREWS, New York I cannot speak from experience, but I have in mind 2 patients who would disprove the remarks of Dr Schwartz about arsenical cancer being caused only by ingestion of arsenic I have 1 patient who has been a copper miner He never took arsenic but got his contact presumably by inhalation He has been under my care for about twelve years, and he has had many typical arsenical keratoses of the palms and soles and also epitheliomas which I have always thought were of arsenical origin

I also have in mind a patient, a woman, who has been throwing sodium arsenate on flower beds as an insecticide for several years and has arsenical keratoses on her hands and face

DR W H GOECKERMAN, Los Angeles We purposely laid particular emphasis on the complications that interested us most so far as this particular patient is concerned I am sure that there could have been more discussion if we had laid emphasis on the various phases of cutaneous lesions, but we saw no object in that, because the literature is now full of articles on this point from different countries But when we became interested in lesions of the mucous membrane we approached the problem with the idea of searching the literature to see how many cases there were of that type, expecting that there would be a large number and at least some in which the lesions had been subjected to microchemical studies So far as we could learn, there were very few reported, and in none had microchemical studies been done

I think that Dr Schwartz's remarks hold water in the main I do not wish to pose as an expert on the toxicology of arsenic, but the literature supports his comments One must always remember, however, that unless the individual cases are investigated it is not known whether the patients are getting arsenic by ingestion or not, because in so many places today there is contamination of the water and food

The whole subject is exceedingly complex As one goes through the literature, one becomes increasingly impressed with this fact

I was glad to hear that Dr Montgomery and Dr Anderson also found cases in which the mucous membrane was involved One cannot help but feel that either this complication is extremely rare or it has not been given the attention it deserves

The thought immediately arose, as we began to work with this problem, that possibly in the cases of a fair percentage of patients without cutaneous lesions, in whom epitheliomas of the mucous membranes develop that are generally accepted as simply the ordinary type of epithelioma, arsenic may be a factor

I think the paper should serve as a stimulant to watch patients from this particular point of view

TREATMENT OF CHANCROID WITH SULFANILAMIDE

ORLANDO CANIZARES, M.D.
NEW YORK

JULIUS A. COHEN, M.D.
BROOKLYN

Therapeutic methods in the treatment of chancroidal infections have ranged from various local measures to the parenteral administration of specific and nonspecific vaccines. Numerous authors¹ have reported favorably on the results obtained with Ducrey vaccines, and for some time the intravenous administration of the specific vaccine was considered the most efficacious procedure available. Its specificity, however, was doubted by some authorities.²

The introduction of sulfanilamide was followed by encouraging reports of its action in infection due to the Ducrey bacillus. In recent reports³ the drug has been considered practically specific for this infection.

From the Department of Dermatology and Syphilology, New York University College of Medicine, and the Department of Dermatology and Syphilology, Third Medical Division (New York University), Bellevue Hospital, service of Dr. Edward R. Maloney and Dr. Frank C. Combes.

1. (a) Dubreuilh, W., and Broustet, P.: *Le traitement du chancre mou par le vaccin de Nicolle*, Ann. de dermat. et syph. **6**:577 (Oct.) 1925. (b) Pardo-Castello, V.: *Chancroid: Its Prevalence; Its Treatment with Specific Vaccines*, Arch. Dermat. & Syph. **28**:155 (Aug.) 1933. (c) Covisa, S., and Gay Prieto, A.: *Contribución al estudio del valor diagnóstico y terapéutico de la vacuna estreptobacilar de Nicolle y Durand*, Arch. de méd., cir. y especialid. **27**:756 (Dec. 31) 1927. (d) Hudelo, A., and Garnier, J.: *La vaccination antichancrelleuse par voie intramusculaire*, Bull. Soc. franç. de dermat. et syph. **35**:760 (July) 1928. (e) Rivalier, G.: *Chancrelle*, in Darier, J., and others: *Nouvelle pratique dermatologique*, Paris, Masson & Cie, 1936, vol. 3, p. 987.
2. Gorlin, D. O.: *Protein-Therapy for Bacillus Ducrey Infections*, New York State J. Med. **35**:729 (July 15) 1935.
3. (a) Kornblith, B. A.; Jacoby, A., and Wishengrad, M.: *Chancroid: Therapy with Sulfanilamide*, J. A. M. A. **111**:523 (Aug. 6) 1938. (b) Beltrami, A.: *La para-amino-fenil-sulfamide nelle affezioni veneree*, Dermosifilografo **13**:488 (Aug.) 1938. (c) Hutchison, A.: *Treatment of Bubo (Chancroidal) with Sulfanilamide*, Lancet **1**:1047 (May) 1938. (d) Grupper, C.: *Infection chancrelleuse et thérapeutique sulfamidée à propos de 24 cas personnels*, Rev. franç. de dermat. et de vénéréol. **15**:175 (April) 1939. (e) Greenblatt, R. B., and Sanderson, E. S.: *Sulfanilamide in Chancroid Disease*, Am. J. Syph., Gonorr. & Ven. Dis. **23**:605 (Sept.) 1939. (f) Schwartz, W. F., and Freeman, H. E.: *Sulfanilamide in the Treatment of Chancroid*, J. A. M. A. **114**:946 (March 16) 1940.

tion However, comparative studies are few Observation at Bellevue Hospital of 182 cases, in 114 of which sulfanilamide was given, within the past three years has enabled us to evaluate the drug from this angle and to establish therapeutic principles for the various manifestations of the disease

In comparing the results of various treatments of chancroidal infections, the size, location and duration of the lesions, the sex, the presence of secondary infection and the variable virulence of the causative organisms are factors to be considered In our opinion multiplicity of the lesions has little effect on the healing process, provided severe edema of the region is not present Sex is important in so far as vaginal secretions provide a favorable medium for bacterial growth The location of the lesions may influence the healing Lesions on the glans penis, anus or labia minora heal slower than cutaneous lesions Phagedenic chancroid in the male occurs almost invariably on the glans penis Secondary infection, virulence of strains and decreased resistance of the patient undoubtedly play a part in the phagedenic destruction of the tissue The association of inguinal adenopathy does not seem to influence the healing of the cutaneous ulcers Therefore, the two types of lesions will be considered separately

The aforementioned factors, however, are too variable to serve as criteria for the classification of cases necessary in a comparative study of therapeutic results The obvious basis for such classification is the size of the lesions Accordingly, our cases were arbitrarily divided into three groups according to the size of the lesions (1) Small chancroids, usually multiple, from the size of a match head to that of a dime, (2) large chancroids, usually single, varying in size from that of a dime to that of a quarter, including irregular elongated lesions of the stellar type and lesions involving the entire circumference of the sulcus, and (3) phagedenic chancroids, invariably single, the size of a quarter or larger, including the deep, destructive ulcers at times simulating carcinoma

The diagnosis of chancroidal infection was based on the negative results of repeated dark field examinations for *Spirochaeta pallida*, positive results of the Ito-Reenstierna test (with no history of previous infection) and/or positive results of autoinoculation Mixed infections with active syphilis or lymphogranuloma venereum and concealed lesions were excluded from this study

The therapy used for the control group was that generally accepted, namely, application of compresses soaked in a 1 to 5,000 solution of potassium permanganate and of iodoform powder and intravenous injections of vaccines The preparations used intravenously were Ducrey and typhoid vaccine The results obtained with them were so much alike that they were classified together We considered their action to be non-

specific. The initial dose of 0.1 cc. was increased gradually and administered every two or three days for a course of seven to eight injections. A severe reaction with fever, malaise and headache usually followed. Rest in bed for seven to ten days was routine in all cases. Patients treated with sulfanilamide received only local applications of dressings wet with saline solution.

In the majority of the cases, sulfanilamide was administered in moderate doses: seventy-five grains (5 Gm.) daily, in divided dosage three times a day, for three days and 45 grains (3 Gm.) daily thereafter. The best results were obtained with this dosage. A few patients received as much as 120 grains (8 Gm.) and others as little as 30 grains (2 Gm.). Sodium bicarbonate was always given simultaneously.

Toxic symptoms in the form of cyanosis, erythema or fever were relatively uncommon. Because of these reactions in 6 instances the administration of the drug was discontinued a few days after the beginning of the treatment. The involution of the lesions continued unhampered.

RESULTS

Chancroids.—In 93 cases the lesions were classified as small chancroids. In 64 of these sulfanilamide was administered. The average time required for cure was twelve days. The condition in the control patients necessitated an average of eleven and six-tenths days to disappear. In 4 cases local therapy failed to control the lesions, which were controlled later by another type of local treatment. This never happened with sulfanilamide.

In the second group were included 68 patients with large chancroids. Sulfanilamide was most efficacious. Thirty-eight patients receiving the drug required eighteen days for cure. In the control group, consisting of 30 patients, the lesions healed in twenty-two and seven-tenths days. In 2 cases of the sulfanilamide group and in 1 of the controls there was relapse.

Group three consisted of 17 patients with phagedenic chancroids. In the control group were 6 patients who were cured in an average of thirty-five days. In 2 cases the lesions relapsed. Eleven patients were treated with sulfanilamide. Six of these healed in a definitely shorter period, of twenty-seven and six-tenths days. However, the remaining 5 did not respond to this form of therapy, necessitating a change to iodiform powder, with resulting cure.

Inguinal Adenopathy.—The patients with inguinal adenopathies were classified in two groups: those with ruptured and those with unruptured buboes. In all the cases rest in bed was given until the acute inflammatory symptoms had subsided. Aspiration of the buboes was performed whenever required.

Of the cases complicated by buboes, in 39 the buboes had not ruptured. The desired effect was accomplished in sixteen days in 20 cases by local therapy in the form of wet dressings, ice bags, the injection of iodoform in glycerin and vaccinothérapie. Nineteen days was necessary in 19 cases in the sulfanilamide series, an evident lack of superiority of this drug in this manifestation of chancroidal infections.

Ruptured buboes were observed in only 12 patients. The 4 control patients healed in an average of fifty-one days. The remaining 8 received sulfanilamide and were cured in a definitely shorter period, twenty-one days.

Effect of Sulfanilamide on Chancroidal Automoculation—Sulfanilamide has a definite action on the Ducrey bacilli. Kornblitt, Jacoby and Wishengrad^{3a} failed to find bacilli in the lesions twenty-four hours after the administration of the drug. In several patients who had a positive reaction to an automoculation test we repeated the inoculation from two to five days after the beginning of the treatment. On every occasion the reaction was negative. The first automoculation healed promptly, without local applications.

CONCLUSIONS

There is no advantage in giving sulfanilamide to patients with small and uncomplicated chancroids. Local therapy seems to be sufficient. If the lesions are not controlled promptly, sulfanilamide is to be given. For large chancroids sulfanilamide associated with local therapy should be used.

In some cases of phagedenic chancroid the result of the treatment by sulfanilamide is striking, in others it is a failure. In all cases, therefore, it should be tried in conjunction with local therapy.

Rest in bed is the most important factor in the prevention of adenopathy in chancroidal infections. When adenopathy is present in the unruptured stage, rest in bed and aspiration of the bubo are of paramount importance. Sulfanilamide does not decrease the formation of pus. On the other hand, the best results with this drug are obtained in patients with ruptured buboes.

Sulfanilamide is therefore of value in the treatment of chancroidal infections. It should not be used, however, in a routine manner, but with knowledge of its value and indications.

FAMILIAL LICHEN PLANUS

A REPORT OF FOUR CASES OF LICHEN PLANUS IN ONE
FAMILY, WITH A BRIEF REVIEW OF THE
LITERATURE

M. H. SAFFRON, M.D.
PASSAIC, N. J.

The inclusion of lichen planus among the familial dermatoses was apparently first suggested by Hallopeau and Leredde¹ in 1900, although several observers, including Lustgarten,² Brocq³ and Ormerod,⁴ had previously reported cases of the disease with a familial background. Lustgarten's original case was published in 1894.

There have been four important résumés of the subject. Jadassohn⁵ in 1900 collected 12 cases from the literature, including 2 from his own practice. Three of these cases were of the conjugal variety. Galewsky⁶ in 1921 reported a total of 31 cases, 26 of the consanguineous variety and 5 of the conjugal type. Spitzer's⁷ comprehensive article appeared in 1924. He carefully reviewed the entire subject, adding 15 cases to the previous report, 3 of these being from his own practice. Juliusberg⁸ covered familial lichen planus in the *Handbuch* in 1931 and presented the arguments for the contagious and neurogenic theories of causation. Montgomery and Culver⁹ reported the second American case

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital.

1. Hallopeau, F. H., and Leredde, L. E.: *Traité pratique de dermatologie*, Paris, J. B. Baillière & fils, 1900.

2. Lustgarten, S.: Three Cases of Lichen Planus in the Same Family, *J. Cutan. Dis.* **12**:501, 1894.

3. Brocq, L.: Quelques considérations sur le lichen ruber planus, *Rev. gén. de clin. et de thérap.* **11**:209, 1897.

4. Ormerod, J. A.: Lichen Ruber Planus, *Brit. J. Dermat.* **12**:413, 1900.

5. Jadassohn, J.: Beiträge zur Kenntnis des Lichen, in *Festschrift gewidmet Moriz Kaposi zum fünfundzwanzigjährigen Professorenjubiläum in Vererbung und Dankbarkeit von Collegen und Schülern*, Vienna, W. Braumüller, 1900, p. 877.

6. Galewsky, E.: Beiträge zur Aetiologie des Lichen ruber: Familiärer Lichen ruber, *Arch. f. Dermat. u. Syph.* **129**:484, 1921.

7. Spitzer, R.: Ueber familiären Lichen ruber planus, *Arch. f. Dermat. u. Syph.* **146**:474, 1924.

8. Juliusberg, F.: Lichen ruber familiaris, in Jadassohn, J.: *Handbuch der Haut- und Geschlechtskrankheiten*, Berlin, Julius Springer, 1931, vol. 7, pt. 2, p. 78.

9. Montgomery, D. W., and Culver, G. D.: Lichen Planus in Two Brothers, *J. Cutan. Dis.* **37**:242, 1919.

in 1919, and Goodman and Sulzberger¹⁰ reporting a case of the conjugal variety brought the literature to date, compiling a total of 57 reported cases

The following are among the more unusual cases reported

Brocq⁸ An acute attack of the disease which developed in a mother while treating a daughter who had lichen planus

Joseph¹¹ Hypertrophic lichen planus in three generations mother, son and grandson

De Azúa¹² Unusual variety of lichen obtusus corneus in a mother and 2 children

Little¹³ Acute lichen planus which developed in 2 sisters, living apart, six weeks after the death of their father

Samuel¹⁴ The annular, atrophic variety in 2 sisters, with the lesions confined to the legs

Bettmann¹⁵ Acute lichen planus in 2 brothers, not living together, characterized by glandular and splenic enlargement

Spitzer⁷ Lichen obtusus corneus in father and daughter, miliary, psoriasiform type of lichen planus in two sisters

Wende¹⁶ Typical lesions of the disease which developed in a 10 month old nursing whose mother had lichen planus

Vonkennel¹⁷ Lichen planus verrucosus in a father and son

Veiel¹⁸ Lichen planus which developed in the father, son and daughter of a family of 4

Scheer¹⁹ Personal knowledge of 3 brothers who had lichen planus

REPORT OF CASES

The F family consists of a father, mother, 4 sons and a daughter. None of the children have lived with the parents or with one another during the past ten years. All members of the family are well educated, sensitive and of above average intelligence

10 Goodman, J, and Sulzberger, M B Conjugal Lichen Planus, Arch Dermat & Syph **35** 1139 (June) 1937

11 Joseph, M Lehrbuch der Hautkrankheiten, Leipzig, Georg Thieme, 1915, p 115

12 de Azúa, J Lichen Planus familiaris vom Typus obtusus corneus, Actas dermo-sif, 1910, no 2, abstracted, Monatsh f prakt Dermat **51** 423, 1910

13 Little, E G G Lichen Planus, J Cutan Dis **37** 639, 1919

14 Samuel, H C Lichen Planus Annularis in Two Sisters, Brit J Dermat **27** 321, 1915

15 Bettmann, S Beitrage zur Kenntnis des Lichen ruber planus, Arch f Dermat u Syph **75** 379, 1905

16 Wende, G W, in discussion on Dade Lichen Planus Acutus, J Cutan Dis **32** 805, 1914

17 Vonkennel, J Lichen ruber verrucosus, Zentralbl f Haut- u Geschlechtskr **30** 691, 1929

18 Veiel, F Lichen ruber als Familienerkrankung, Arch f Dermat u Syph **93** 383, 1908

19 Scheer, M, in discussion on Feit, H Lichen Planus in Mother and Child, Arch Dermat & Syph **20** 254 (Aug) 1929

Acute lichen planus developed in Mrs. F. F., a housewife aged 52, in May 1921, involvement being especially pronounced on the legs and the upper part of the abdomen. Oral lesions were numerous. Pruritus was intense. The attack was gradually controlled by arsenic taken internally and subsided in October of the same year. In September 1936 she suffered a severe recurrence of lichen planus. Again the lower extremities and the abdomen were the chief sites of the eruption. Mercury salicylarsenate, (enesol), a bismuth compound and roentgen rays were used in controlling this attack, which lasted for eight months. At the last observation (1939) there were still areas of pigmentation on the legs.

R. F., a salesman aged 36, had lichen planus in 1932. The lesions were few and involved the penis, upper part of the abdomen and oral mucosa. Pruritus was slight, and the lesions disappeared, after the administration of solution of potassium arsenite U. S. P., in approximately three months.

S. F., a dentist aged 37, had lichen planus in 1936. The lesions were confined to the penis, forearms and oral mucosa. Treatment consisted of administering a bismuth compound and injections of enesol. Severe pruritus required localized roentgen ray therapy. The attack subsided about six months after the onset.

A. F., a factory manager aged 38, had an acute, widespread eruption of lichen planus in 1938. The lesions covered large portions of the body. The skin appeared edematous and inflamed. Pruritus was intense. Therapy consisted of rest, sedation and wet dressings. Later mercury salicylarsenate (enesol) was used, with success. The entire course of this attack was approximately twelve weeks, after which a few chronic lesions remained on the forearms and legs. In May 1939 he suffered a severe relapse, resembling in every respect the earlier attack. In March 1940 there were still a few pigmented spots on the upper and lower extremities and a few oral lesions.

SUMMARY

This is the first reported instance of lichen planus in 4 members of one family.

To date 60 cases of familial lichen planus have been reported in the literature, 50 of the consanguineous variety and 10 of the conjugal.

It is suggested that all patients with lichen planus should be questioned as to other cases in the family. Statistics of such a nature may assist in establishing a neurogenic cause for the disease, which the present report suggests.

Clinical Notes

MOIST PAPULES IN THE AXILLA

SYDNEY GELLIS, M D, AND SAMUEL BLUEFARB, M D, NEW YORK

Moist papules are most frequently found about the female genitalia, in the groins and on the apposing surfaces of the thighs. Since among hundreds of cases observed in our service the following case was the first in which lesions of this kind in the axilla were seen, we think it interesting enough to report.

REPORT OF A CASE

M W, a white woman aged 54, was admitted to Bellevue Hospital complaining of sores around the genitalia of one month's duration. The patient was



Moist papules in the axilla

an alcoholic addict and admitted sexual promiscuity. She had been married twice. A pregnancy, which occurred eighteen years prior to admission, terminated in a stillbirth. She stated that the Wassermann reaction was negative six years ago. On admission the patient complained of a sore throat of six weeks' duration. About two weeks after the sore throat developed she noticed "pimples on the face" and sores around the genitals. She also noticed "pimples in the left arm pit," which first appeared three weeks after the development of the sore throat.

Examination revealed injection of the fauces. No mucous patches were present. A papular eruption with induration was seen on the face, wrists and soles. There were moist papules about the anus and vulva. In the left axilla two split pea-sized smooth papules with moist surfaces were observed. The vaginal examination gave negative results. No other constitutional signs or symptoms were recorded.

From the Department of Dermatology and Syphilology, New York University College of Medicine, and the Department of Dermatology and Syphilology, Medical (N Y U) Division, Bellevue Hospital, service of Dr. Edward R. Maloney.

The dark field examination of material from lesions around the vulva and from lesions in the left axilla showed spirochetes. The Wassermann reaction of the blood was 4 plus. The Frei test and the Ito-Reenstierna test gave negative results. Histologic examination of a papule in the left axilla revealed characteristic changes of syphilis.

The lesions responded rapidly to antisyphilitic treatment and became dark field negative twenty-four hours later.

SUMMARY

A case in which there were the cutaneous features of secondary syphilis and moist papules in the left axilla is reported.

RECKLINGHAUSEN'S DISEASE IN IDENTICAL TWINS

EARL L. LOFTIS, M.D., DALLAS, TEXAS

Though the familial occurrence of Recklinghausen's disease has long been established, many examples in both sexes of the same and succeeding generations of predisposed families having been reported, I have not found a report of its presence in twins.

REPORT OF CASES

Identical twins, unmarried women aged 42, consulted me about an eruption which had been present since the age of 8 years. The condition appeared simultaneously in the patients and has slowly progressed, new lesions appearing from time to time. The eruption now consists of hundreds of soft, fleshy and elevated tumors scattered over the face, neck, chest, arms and back. The tumors have about the same distribution in the twins. They vary from the size of a pinhead to that of a dime and from the color of normal skin to dark brown. Many of the tumors can be invaginated, and some are apparently cystic. No tenderness or pain is present. None have disappeared, as far as the patients know. On the forearm of one is a light brown nonelevated spot, 2 inches (5 cm.) in diameter, and on the other there is a similar spot in the lumbar region, each of which has been present since infancy. One of them has a tumor on the vocal cord, the other an increasing deafness in both ears which has been present about ten years. The intelligence of the patients is of low average. The family history is negative for similar conditions back to the second generation. The histologic picture is typical of Recklinghausen's disease.

1502 Medical Arts Building.

Submitted for publication May 20, 1940.

News and Comment

PROGRAM NOTICE

Applications for places on the program of the Section on Dermatology and Syphilology for the Annual Session of the American Medical Association at Cleveland, June 2 to 4, 1941, are now being received. All Fellows of the Association are eligible. The program is usually assembled in the early part of December. Essayists who are not Fellows of the Association may be accepted by invitation.

All applications should be addressed to Dr. C. F. Lehmann, Secretary of the Section on Dermatology and Syphilology, 705 East Houston Street, San Antonio, Texas.

PACIFIC NORTHWEST DERMATOLOGICAL SOCIETY

On Oct. 19, 1939 dermatologists from Portland, Ore., Seattle, Tacoma and Spokane, Wash., and Vancouver, British Columbia, Canada, held a meeting at Vancouver and organized the Pacific Northwest Dermatological Society. They elected Dr. Lyle B. Kingery president and Dr. John H. Labadie secretary-treasurer for the ensuing year, both being from Portland. A constitution and set of by-laws were drawn up and adopted.

It was decided that the next meeting of the society should be held in Portland, and on May 9, 1940 the second meeting of the group took place in that city. After the presentation of about 40 cases at the University of Oregon Medical School, outpatient department, a business meeting was held and was attended by 24 dermatologists from the five cities. Dr. Lyle B. Kingery was re-elected president, Dr. Richard J. Bailey, Spokane, vice president and Dr. Robert L. Howard, Spokane, secretary-treasurer for the ensuing year.

The next meeting of the society is to be held in October 1940 in Spokane.

MICROFILM COPYING

Microfilm copying of the original articles referred to in this journal and published in the periodicals received by the Army Medical Library of Washington, D. C., is being done by "Medicofilm Service," a nonprofit organization operating in the Army Medical Library. The charge is 30 cents for each complete article not exceeding thirty pages in length and 10 cents for each additional ten pages or fraction thereof. A circular of information containing a list of the more than 4,000 periodicals received by the Army Medical Library will be sent on request. Orders and remittances should be sent to Medicofilm Service, Army Medical Library, Seventh Street and Independence Avenue, South West, Washington, D. C.

CORRECTION

In the article by Dr. Frances Pascher entitled "Exudative Chronic Discoid and Lichenoid Dermatitis (Sulzberger and Garbe)," in the August issue (*ARCH DERMAT & SYPH* 42:322, 1940), in the fourth line from the end of the first paragraph on page 331, "Exsiccated sodium arsenate N. F." should have read merely "Sodium arsenate."

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

OCCURRENCE OF MONILIA IN NORMAL STOOLS. T. G. SCHOONER, *Am. J. Trop. Med.* **19**:163 (March) 1939.

Schooner studied the stools of a series of 314 normal persons by making cultures to determine the frequency of fungi in their gastrointestinal tracts. *Monilia* was found in 33.1 per cent of the stools cultured. As to types, *Monilia albicans* occurred in 16.9 per cent, *Monilia parapsilosis* in 6 per cent, *Monilia krusei* in 5.7 per cent and *Monilia candida* in 4 per cent. Other fungi isolated and identified were: *Cryptococcus*, in 28 per cent; *Geotrichum*, in 29 per cent; *Penicillium*, in 11.8 per cent, and *Aspergillus*, in 3.5 per cent.

BURPEE, Augusta, Ga. [*AM. J. DIS. CHILD.*]

IDIOPATHIC FAMILIAL LIPEMIA. L. EMMETT HOLT JR., FRANCIS X. AYLWARD and HARRY G. TIMBRES, *Bull. Johns Hopkins Hosp.* **64**:279 (May) 1939.

A girl, aged 11 years, had extreme lipemia due primarily to neutral fat and associated with hepatomegaly, splenomegaly, psoriasis, peculiar ulcerations of the skin and malnutrition. Periodic acute attacks of abdominal pain occurred, accompanied by a sudden reduction of fat in the blood, enlargement of the liver and spleen and engorgement of the abdominal veins. There was evidence that the disorder was familial.

The condition was not improved by lecithin, choline, thyroxin, insulin, "lipocaic" or anterior pituitary therapy. It could, however, be in large measure controlled by a diet low in fats. Some evidence was obtained of a beneficial effect of transfusion.

The various types of disturbance which may give rise to lipemia are discussed. It is suggested that the condition described is due to a defective mechanism for removal of fat from the blood by the liver, a mechanism in which a humoral factor appears to be concerned.

FROM THE AUTHOR'S SUMMARY. [*AM. J. DIS. CHILD.*]

THE ANTI-ACRODYNIC PROPERTIES OF CERTAIN FOODS. HOWARD A. SCHNEIDER, J. KATHERINE ASCHAM, BLANCHE R. PLATZ and H. STEENBOCK, *J. Nutrition* **18**:99 (July) 1939.

These Wisconsin investigators have assayed fifty-two foodstuffs for their anti-acrodynamic activity (antidermastic factor, vitamin B₆), using the rat as the experimental animal. Their data show that certain vegetable fats are extremely potent sources of antiacrodynamic activity; fruits and vegetables are poor; meats and fish are fair and seeds, legumes and cereals are relatively rich. Yeast shows about the same potency as the cereals. Lard is actually six times as potent as yeast.

FREDEEN, Kansas City, Mo. [*AM. J. DIS. CHILD.*]

A CASE OF ALEUKAEMIC LYMPHOSIS INVOLVING THE UPPER LIDS WITH PATHOLOGICAL FINDINGS. F. TOOKE, *Brit. J. Ophth.* **23**:444 (July) 1939.

A man aged 65 was admitted to the hospital with a pendulous right lid. A tumor was presented. The skin of the lid was not discolored and was movable over the underlying tumor. The palpebral conjunctiva was thick, lusterless and pinkish gray, resembling somewhat sodden blotting paper. The upper lid of the left eye presented practically the same features. Except for a moderate degree of chemosis about the accessory lacrimal glands, the globes appeared normal.

There was a uniform adenopathy. A roentgenogram showed marked enlargement and increased density involving the roots of both lungs. This may have been due to hypertrophied glands. Biopsy of the tumors and of the posterior cervical glands gave a picture corresponding to that found on the borderline between lymphatic leukemia and a relatively mature form of lymphosarcomatosis. The author is inclined to classify the disease among the rather immature forms of lymphatic leukemia. The blood picture showed evidence of marked anemia, with a tendency for the cells to be somewhat larger than normal and to have poor regenerative ability. The white blood cells showed deficiency in the number of the myeloid elements, with some immature forms. The lymphocytes were increased, the increase appeared to be due to the presence of immature lymphoblastic cells, corresponding to those to be met with in the lymph glands.

The concluding paragraph of the article contains the following statements:

"This case, therefore, is one of a systemic lymphoid proliferation, which apparently from the progressive changes in the blood picture has involved the bone marrow, spleen, and lymph glands of the patient, as well as in an unusual manner, the eyelids. The proliferation is of a comparatively active form, and falls in its intensity and character between that met with in lymphatic leukaemia and that in lymphosarcomatosis. For this reason it is best classified as a leukaemic form of lymphosis, with unusual involvement of the eyelid and with an activity of cell proliferation bordering on the lymphosarcomatoses."

ZENTMAYER, Philadelphia [ARCH OPHTH]

HERPES SIMPLEX F. M. BURNET and DORA LUSH, *Lancet* 1 629 (March 18) 1939

Herpes antibody in human serums can be titrated on the chorioallantois. With few exceptions human serums either contain no herpes antibody or are highly active against the virus. There is no relation between susceptibility to clinical poliomyelitis and absence of herpes antibody. Herpes virus could not be demonstrated post mortem in the gasserian ganglions of persons with high titer herpes antibody. Aphthous stomatitis in infancy is the common manifestation of primary infection with herpes virus. Primary herpes is an infective disease spread by droplet infection or by salivary contamination, particularly in children aged from 1 to 3 years.

As a working hypothesis the authors adopt the view that, once maternally transmitted immunity has been lost, there is a period roughly from 9 months to perhaps 5 years of age during which the child is readily susceptible to infection of the buccal mucosa by herpes virus. Once infection has been acquired, the virus persists in certain cells throughout life and provokes its characteristic manifestation, labial herpes, when conditions are suitable.

LANGMANN, New York [AM J DIS CHILD]

RESULTS OBTAINED IN LUPUS ERYTHEMATOSUS BY INOCULATING THE BLOOD INTO MONKEYS L. M. PAUTRIER and R. GLASSER, *Bull Soc franç de dermat et syph* 46 1105 (Sept-Oct) 1939

The authors studied 30 cases of lupus erythematosus in an attempt to prove a tuberculous causation. Four fragments of tissue from the lesions and 30 specimens of blood were inoculated into 19 monkeys in one series of experiments and into 160 animals in a second series. Autopsies were performed on the animals, and the organs were systematically examined histologically and bacteriologically. No tuberculous lesions could be demonstrated.

LAYMON, Minneapolis

THERAPEUTIC RESULTS IN ONE HUNDRED CASES OF EPITHELIOMA OF THE LID TREATED BY IRRADIATION AT THE RADIUM INSTITUTE OF PARIS BETWEEN 1935 AND 1937 M. A. DOLLFUS, *Bull Soc d'opht de Paris* 51 27 (Jan) 1939

Of 100 patients with epithelioma of the lid, 38 were treated in 1935, 32 in 1936 and 30 in 1937. Thirty-six growths were located at the internal canthus, 26 at the

interior of the lid, 13 contiguous with the nose, 9 under the orbit, 8 above the orbit and in the region of the eyebrow, 3 on the upper lid, 3 at the corneal limbus, 2 at the external angle and 1 in the orbital cavity. Fifty-seven of the patients were women and 43 men. Radium was used in 96 cases, roentgen rays with radium in 3 cases and telerradium therapy in 1 case, for an enormous epithelioma of the orbit. The technic is explained in full, and the methods used to guard against injury to the eye from the rays are detailed. Eighty-eight patients were considered cured. Complications existing in the eye or its adnexa did not entitle 10 of the patients to be registered as cured. Extension of the initial lesion in 2 patients could not be halted. With proper care and protection of the eyeball, irradiation is preferred to operation because of less chance of ugly scar formation.

MAYER, Chicago. [ARCH. OPHTH.]

SYPHILITIC CHANCRE ACQUIRED BY A NEWBORN INFANT DURING DELIVERY.
G. NASTASE, Bull. Soc. de pédiat. de Iasi 9:40, 1938.

A chancre developed on the scalp of an infant during the third week of extra-uterine life. Secondary lesions of the skin and mucous membranes were present when the child was 2 months of age. The mother was suffering from secondary lesions at the same time; she stated that these had been present for thirty days. The mother had been infected during the eighth month of pregnancy. The placenta must have been an effective barrier to the transmission of infection during intra-uterine life.

LESLIE, Evanston, Ill. [AM. J. DIS. CHILD.]

PHOTOSENSITIZATION AND MELANODERMIA CAUSED BY MERCUROCHROME. MARCIAL
I. QUIROGA, Rev. méd. latino-am. 24:472 (Feb.) 1939.

A young woman received daily intravenous injections of mercurochrome for six consecutive days. The first dose was 2 cc., the daily dose being increased by 0.5 cc., so that the final amount was 4.5 cc. The injection was given about noon daily, and shortly thereafter the patient would expose herself to the sun for one to one and one-half hours. After the third injection an eruption appeared on the legs, hands, forearms and face. In addition there was considerable swelling of both cheeks. There was stomatitis, the buccal mucosa being reddened, and there was profuse salivation. The eruption lasted about two weeks, and when it disappeared, there remained a brownish pigmentation which has persisted with gradual improvement for two months.

The author states the belief that the condition was caused by the photosensitizing action of the dibromofluorescein contained in the mercurochrome on the epidermal cells.

LEIFER, New York.

EVALUATIONS OF VITAMINS A, B₁ AND C AS THERAPEUTIC AGENTS. S. KUTHAN,
Wien. klin. Wchnschr. 25:597 (June 23) 1939.

If investigators wish to evaluate the therapeutic effectiveness of vitamins A, B₁ and C, they cannot help but be disappointed occasionally if the use of these vitamins is not strictly confined to conditions for which they are specific, according to Stephen Kuthan. With the use of vitamin C, he obtained fairly good results in treating hemorrhagic stomatitis and gingivitis accompanying various diseases. He also obtained favorable results in treating hemorrhagic diathesis in certain cases. He states that other therapeutic indications for this vitamin are questionable.

He obtained good results by using vitamin B₁ in cases of alcoholic neuritis and in neuritis accompanying gastrointestinal disturbances, but in treating other conditions the results with vitamin B₁ were questionable.

Vitamin A proved most valuable in those conditions in which a disturbance in the mucosal epithelium was evident.

He states that he does not wish to minimize the therapeutic value of these vitamins, and he also points out that to the aforementioned specific conditions one

must add the various latent hypovitaminoses. In other words, a deficiency in the intake of the aforementioned vitamins, although not giving rise to clinical manifestations of disease, may play a part in the production of certain disease conditions. The question of resistance to avitaminosis as produced by Georges and Mouriquant has not yet been fully investigated. He emphasizes the fact that in certain conditions therapy with vitamins A, B₁ and C must be augmented by other indicated therapeutic agents.

ABT, Chicago [AM J DIS CHILD]

TWO CASES OF OSTEOPERIOSTOPATHIA HYPERTROPHIANS SECUNDARIA ASSOCIATED WITH PERNIONES ATUSI NAKAZYO, *Jap J Dermat & Urol* 45 25 (Feb) 1939

The author reports the condition of osteoperiostopathia hypertrophians secundaria (described in 1890 by Pierre Marie) in a brother and a sister whose parents were blood relatives. Both children had a compensated congenital cardiac defect and thickening of the distal ends of the body, like the nose, ears, chin and particularly the ends of the fingers and toes. There was also thickening of the periosteum of the long bones. These areas showed also perniones, which could readily be produced artificially. The author considers all these changes as secondary changes due to the heart defect, which caused stasis in the capillaries and proliferation of the soft parts and bones. The production of the perniones is explained in the same way.

DIETETIC TREATMENT OF PSORIASIS VULGARIS K TAKENOUTI, *Jap J Dermat & Urol* 45 32 (Feb) 1939

The author has treated 3 patients with psoriasis vulgaris successfully with the diet of Grutz, which contained 60 Gm of protein, 4 to 6 Gm of fat and 400 Gm of carbohydrates, amounting to about 2,000 calories. The remaining few obstinate lesions had to be treated locally or by administration of a gold compound.

In all 3 cases histochemical examination revealed a moderate deposition of fat and lipid substance in the epidermis and cutis. Serum cholesterol showed a typical psoriasis curve when the Belastung test of Burger was used. The serum cholesterol figures rose parallel with the exacerbation of the eruption.

CLINICAL OBSERVATIONS OF THE PRIMARY LESION IN LYMPHOGRANULOMA VENEREUM T ITIKAWA and R SHINODA, *Jap J Dermat & Urol* 45 79 (April) 1939

The authors found a primary lesion in 36 per cent of the cases of lymphogranuloma venereum. They have observed different forms of primary lesions: (1) the herpetic lesions, (2) the papular and the ulceropapular, (3) the nodular and the ulceronodular and (4) urethritis. The lesion may be solitary, or two to three lesions may be present. Different forms of primary lesions may be seen in the same person. The fact that the primary lesion heals rapidly explains why in two thirds of the cases it is not observed. The rapid healing of the herpetic lesion or its change into the papular or nodular form accounts for the fact that these forms of primary lesion are seen more frequently than the herpetic form. Only a small percentage of primary lesions appear from the start as papules or nodules.

CONTRIBUTION TO THE KNOWLEDGE OF "CHRONIC POLYMORPHOUS ERUPTIONS DUE TO LIGHT" S OHMORI, *Jap J Dermat & Urol* 45 81 (April) 1939

The author reports the case of a man aged 25 who suffered a recurrent papulovesicular eruption on the face, neck and hands after exposure to the sun. Investigation revealed that the patient's skin was sensitive to the visible light rays, particularly to the green part of the sunlight. Dysfunction of the liver was proved not only indirectly, by the finding of urobilin and urobilinogen and an excess of coproporphyrin in the urine, but also directly by liver function tests. There was

hypersensitivity of the vegetative nervous system to pilocarpine. The author succeeded in diminishing the photosensitivity of the skin in the patient by means of intravenous administration of a 10 per cent solution of sodium thiosulfate together with large doses of a liver preparation (yakriton).

THE INFLUENCE OF DERMATITIS SERUM ON ANTIBODY FORMATION. I. MIYAKE and K. YOSHIOKA, *Jap. J. Dermat. & Urol.* **45**:101 (May) 1939.

Animal experiments revealed that antibody formation stimulated by injection of egg albumin is greatly increased when blood serum from rabbits with dermatitis is added to the egg albumin. The serum taken on the fifth day of the dermatitis proved to be moderately active; that on the fourteenth day, intensely active, and that on the nineteenth day did not enhance any antibody formation at all. These observations lead to the conclusion that the serum of rabbits with dermatitis contains a substance which stimulates the formation of antibodies.

THE PRIMARY LESION OF LYMPHOGRANULOMA VENEREUM: SECOND REPORT. R. SHINODA, *Jap. J. Dermat. & Urol.* **45**:103 (May) 1939.

Histologic examination of different forms of primary lesions of lymphogranuloma venereum revealed nonspecific exudative and proliferative changes in the herpetic form, lymphoma and proliferation of reticuloendothelial cells in the papular-ulcerative form and microabscesses in the nodular-ulcerative form. Material from 30 primary lesions of 32 was successfully inoculated into the brains of mice. A Frei antigen could be prepared from 5 primary lesions, although it was less effective than the usual Frei antigen prepared from the pus of the inguinal bubo. However, the nodular primary lesion gave as effective an antigen as that of the bubo. When pus of the bubo was injected into the skin of control patients, a primary lesion was produced, which healed in most instances after eight days. In 4 cases the infiltration persisted for fourteen days, and in 1 case it persisted for four weeks and changed into an ulcer which resembled the nodular-ulcerative form of primary lesion. Only in 2 cases of 22 was there associated lymphadenitis, although the Frei test gave a positive reaction in all 22 cases. This observation shows that there may be infection with lymphogranuloma venereum without concomitant bubo formation.

BLOOM, New York.

STUDIES ON SECRETION OF SWEAT IN THE NEWBORN. SHIGESHI UCHINO, *Jap. J. Obst. & Gynec.* **22**:9 (Jan.) 1939.

Twenty-eight of 57 full term infants first showed evidence of secretion of sweat from two to eighteen days after birth. In 15 per cent of the 28 secretion occurred between the third and the fifth day. In 4 infants born between the thirty-fourth and the thirty-seventh week of pregnancy sweat first appeared from thirteen to twenty-four days after birth. One showed no evidence of secretion thirty-three days after birth.

Pilocarpine injected into the skin of infants born as early as the twenty-eighth week of gestation gives local secretion of sweat. Absence of the secretion after birth is due to immaturity of the center controlling secretion and not to inability of the glands to secrete. ADAIR and POTTER, Chicago. [*Am. J. Dis. Child.*]

CLINICAL INVESTIGATION OF ARSPHENAMINE EXANTHEMS: I. STATISTICAL INVESTIGATION OF ARSPHENAMINE EXANTHEMS. K. AKIYAMA, *Lues: Bull. Soc. japon. de syph.* **17**:173 (Dec.) 1938.

The author has observed, from 1921 to 1937, 108 cases of arspenamine eruption, excluding melanosis and fixed eruption. Most frequently the eruption appeared after the second injection, less frequently after the first and third and still less frequently after the sixth to the tenth injection. The most frequent types

of eruption are erythema, eczema and erythroderma. Only 25 per cent of the patients with early erythema tolerated further treatment with arsphenamine. Twenty-five per cent of them had recurrence with each further injection, and 50 per cent reacted to further treatment with severe dermatitis. Early erythema may sometimes change to papular or vesicular eczematous eruption when further arsphenamine administration is continued. The eczematous form may sometimes appear early, but usually it appears late. To the atypical erythemas belong eruptions resembling pityriasis rosea, lichen planus, lupus erythematosus and less often erythema nodosum. The severe form of arsphenamine dermatitis appears as exfoliative erythroderma and rarely as a vesicular or hemorrhagic eruption. "Late dermatitis," which develops two to three months after arsphenamine has been administered, has not been observed by the author. To the late reactions belongs also the disseminated hyperkeratotic eruption which may resemble Darier's disease. Arsphenamine melanosis and so-called arsphenamine ichthyosis are mostly results of a usual arsphenamine dermatitis. They are extremely obstinate to treatment but may respond to the administration of ascorbic acid.

IMMUNOLOGIC INVESTIGATIONS, PARTICULARLY OF THE LYSIN, IN THE CEREBRO-SPINAL FLUID OF TABETIC PATIENTS INFECTED WITH RELAPSING FEVER
T. YAMASHITA, Lues Bull Soc japon de syph 18 19 (Feb) 1939

Animal experiments reveal that a lysin which has a damaging effect on *Spirochaeta pallida* is present in the cerebrospinal fluid of patients with tabes who have been infected with relapsing fever. This lysin substance is, however, much weaker than that found in the serum of these patients.

ON THE ERYTHROCYTE SEDIMENTATION RATE AND THE CHOLESTEROL CONTENTS OF THE BLOOD SERUM IN YAWS K. NAGASAKI, Lues Bull Soc japon de syph 18 31 (Feb) 1939

Investigation of healthy persons and those affected with yaws on the island of Ponape revealed the following facts. The average erythrocyte sedimentation rate in persons affected with yaws was accelerated in the second stage of the disease and more so in the third. In the course of arsphenamine administration the sedimentation rate diminished. The average cholesterol content in the blood serum in persons with yaws was only slightly higher compared with that of normal people. When it was high it diminished gradually during treatment with arsphenamine. There was no connection between the cholesterol value and the serologic reaction or the rate of sedimentation.

BLOOM, New York

PRIMARY TUBERCULOUS INFECTION OF THE SKIN N. DANBOLT, Norsk mag f lægevidensk 99 44 (June) 1938

The patient, a girl aged 12 years, suffered a traumatic lesion of the left elbow, and two weeks later the lymphatic glands of the axilla swelled. The lesions did not heal. Five weeks after the trauma erythema nodosum appeared. Pirquet's reaction was present. There was fever for some weeks. The ulceration healed eventually, but at the site lupus developed. This was extirpated at the dermatologic clinic. Histologic examination showed tuberculosis.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

E. WILLIAM ABRAMOWITZ, M.D., *Chairman*

LEWIS B. ROBINSON, M.D., *Secretary*

Feb. 14, 1940

Symposium on Syphilis

Acute Hemorrhagic Encephalitis Due to Neoarsphenamine, with Recovery. Presented by DR. NATHAN SOBEL.

M. R., a man aged 28, a clerk, is presented for Dr. Nathan Pensky, to whom he was referred on Oct. 1, 1939, because of a 4 plus Wassermann reaction. He stated that he had never had a venereal disease but gave a history of a quiescent duodenal ulcer. Physical examination at that time showed that the right pupil was slightly unequal and reacted sluggishly to light. Otherwise, the central nervous system and the heart were normal. The Wassermann reaction of the blood was 4 plus on three successive examinations. At that time the patient refused to allow a lumbar puncture.

Therapy was instituted with bismuth in oil in doses of 2 cc. once a week for five weeks. This was well tolerated. In the sixth week 0.3 Gm. of neoarsphenamine was administered. One week later 0.45 Gm. of the same preparation was given, without any immediate reaction. The next morning, however, the patient had chills, headache, dizziness and weakness and remained home from work. On the following day he felt better and went to work but returned home not feeling well. On the third morning he arose and began to dress but felt peculiar. He stared into space for a short time and then had a convulsion, followed by vomiting of material the color of coffee grounds. The patient was then admitted to Beth Israel Hospital, with the diagnosis of acute hemorrhagic encephalitis.

Examination on admission to the hospital showed absence of all the deep reflexes of the lower extremities and diminution of the deep reflexes of the upper extremities. The pupillary findings were the same as previously mentioned. The patient was comatose and assumed a fetal-like position. No meningeal signs were noted. The blood pressure was 100 systolic and 70 diastolic. The temperature was 99 F. and the pulse rate 110 per minute.

Lumbar puncture showed a slight increase in pressure. The fluid was clear and contained 16 cells per cubic millimeter, of which 14 were lymphocytes and 2 were polymorphonuclear leukocytes. Total protein amounted to 77 mg. and dextrose to 40 mg. per hundred cubic centimeters. Urinalysis showed a 2 plus reaction for albumin, a trace of acetone, granular casts and 1 to 2 red blood cells per high power field. A blood count showed 26,000 leukocytes per cubic millimeter, with a differential count of 90 per cent polymorphonuclear leukocytes and 10 per cent monocytes; the hemoglobin amounted to 104 per cent. The bleeding time and coagulation time were normal. Chemical examination of the blood showed 166 mg. of sugar and 36 mg. of nonprotein nitrogen per hundred cubic centimeters. The analysis of the vomitus showed a 4 plus reaction to a benzidine test.

The patient was given 1 cc. of solution of epinephrine hydrochloride every three hours intramuscularly, hypertonic solution of dextrose intravenously and clyses. On the night of admission the temperature rose to 104 F. On the follow-

ing day it returned to normal. On the third day the patient emerged from his stupor and was able to recognize his wife. At that time there was diminution of the reflexes of the lower extremities with the exception of the left achilles reflex, which was absent. The right patellar reflex was weaker than the left one. For the following seven days the patient complained of headaches and dizziness, after which he became symptom free. The urine became normal. The blood showed a persistent eosinophilia, with 7 to 10 per cent eosinophils. Roentgenograms of the gastrointestinal tract showed a duodenal ulcer. Lumbar puncture was repeated and showed 1 cell (polymorphonuclear leukocyte) per cubic millimeter and 30 mg of dextrose and 700 mg of chlorides per hundred cubic centimeters. The Wassermann reaction was positive down to 0.2 cc., and the colloidal gold curve read 1233100000. At this time chemical examination of the blood showed 82 mg of dextrose and 33 mg of nonprotein nitrogen per hundred cubic centimeters.

The patient was discharged from the hospital on December 28. On Feb 7, 1940 all the reflexes were normal with the exception of the achilles reflex.

DISCUSSION

DR LOUIS CHARGIN. Fortunately this complication is rare, yet I have encountered 6 cases, and I do not think that the prognosis is necessarily bad. Several years ago the subject was fully discussed by Glaser, Immerman and Immerman (*Am J M Sc* 189 64 [Jan] 1935). The reports they collected from the literature showed a mortality rate of 76 per cent. In the cases that I have observed the mortality rate was only 50 per cent. If the process is severe, with the cord or meninges affected, and if the patient fails to show improvement by the fourth day, the prognosis is usually bad. On the other hand, if improvement appears by the third day, the outlook is good, and recovery when it occurs is complete. The case presented this evening is an example of this. I do not know what causes this complication, but I do not know that this condition does not occur following the first injection but as a rule follows the second injection and may follow subsequent injections. There seems to be no way of determining the sensitivity beforehand. Two signs that appear early stand out and should be watched for in all patients receiving trivalent arsenicals. The first one is convulsions, and the second, a change in mentality which manifests itself by a state of confusion. As soon as either sign appears, treatment should be instituted at once. Treatment consists of repeated lumbar punctures and dehydration by the intravenous injection of a 50 per cent solution of dextrose.

DR A. BENSON CANNON. I agree with Dr Chargin, and I should like to add that of the 4 patients that I have had in private practice all have recovered after rest in bed and daily drainage of spinal fluid. I recall a most interesting patient, a man 72 years old, in whom acute hemorrhagic encephalitis developed after his second injection of neoarsphenamine. He was maniacal, difficult to restrain and so ill that the neurologic consultant predicted death within a few hours. The Kernig sign, ankle clonus and Babinski signs were present on both sides, and he had strabismus, inequality of the abdominal reflexes and incontinence. On the fourth day the man regained consciousness, and on the fifth day he went to Atlantic City, N. J., to recuperate. The other 3 patients were treated in the same way, and each in turn recovered in from four to seven days and later received alternate courses of arsphenamine and a heavy metal, without reactions. In 1 of these patients a second infection developed several years later, which was again cured with arsphenamine and a heavy metal. While encephalitis is undoubtedly a serious complication, probably being the result of an anaphylactic reaction to the arsphenamine, I do not believe that the condition is as serious as most physicians lead one to suspect, provided the patient is promptly hospitalized and repeated drainages of spinal fluid are performed. In all 4 of my cases the fluid was under considerable pressure.

DR FRANK E. CROSS (by invitation). I know of a young man with early syphilis in whom acute hemorrhagic encephalitis developed after his second injection of neoarsphenamine and who made a complete recovery.

SOCIETY TRANSACTIONS

DR. LEO SPIEGEL: Why is this condition called hemorrhagic encephalitis? Why not call it encephalitis? It either is an anaphylactic reaction or is due to some toxemia. The results of examination of the spinal fluid do not show any xanthochromia or any red blood cells. May I ask the presenter to discuss this question?

DR. E. WILLIAM ABRAMOWITZ: I understand exception has been made to the use of the term encephalitis in this condition. It is more of a purpura affecting the cerebral vessels.

DR. NATHAN PENSKY (by invitation): This patient was presented because of his recent recovery from an acute involvement of the central nervous system following arsenical therapy and because of the problem of future management. There are several points in this case of acute hemorrhagic encephalitis that I feel are of importance. The patient had no meningeal signs, but damage to the nervous system was evident. The spinal fluid pressure was increased; the blood sugar was elevated (166 mg. per hundred cubic centimeters), owing to irritation of the brain centers; a fetal-like attitude was assumed by the patient during his period of unconsciousness, and there were changes in his reflexes. The prognosis in these cases depends on the severity and type of involvement. Patients who show only encephalitic involvement have a better prognosis than those with a myelitic or encephalomyelitic picture, who have practically 100 per cent mortality rate. Though the outstanding feature of this syndrome is the involvement of the central nervous system, it must not be forgotten that the condition is a systemic one. There are pathologic changes found in many organs of the body, including the liver, spleen and, particularly, the kidney. In my case the urine showed a 2 plus reaction for albumin and many red blood cells, which subsequently disappeared.

Dr. Spiegel asked whether the name hemorrhagic encephalitis is a proper one. The name is a misnomer, and many descriptive terms have been used, none of them being entirely satisfactory.

DR. E. WILLIAM ABRAMOWITZ: What is the bearing of the duodenal ulcer in connection with the development of this syndrome?

DR. NATHAN PENSKY (by invitation): Fever therapy was considered as a possible future procedure in treating the syphilis of the central nervous system in this patient. In view of the duodenal ulcer, which was activated during his illness, and the severe insult to his system, however, I doubt whether fever therapy should be considered at all.

DR. E. WILLIAM ABRAMOWITZ: Was the blood taken for the examination for sugar before or after the epinephrine was given?

DR. NATHAN PENSKY (by invitation): I am not positive but I believe that the blood was taken for the first determination before therapy was instituted.

Bilateral Paralysis of the Abducens Nerve Following Lumbar Puncture.

Presented by DR. LEO SPIEGEL.

M. P., an Italian aged 36, is presented from Bellevue Hospital. He gives a history of having had a sore on the penis in 1922. He began receiving antisyphilitic treatment in 1929, when he had twelve intramuscular and six intravenous injections. He continued treatment again in 1932, off and on. During the past six months he has received only injections of mercury, his last treatment being two months before the lumbar puncture, which was performed at the West Side social hygiene clinic of the department of health on Jan. 9, 1940. The Wassermann reaction of the blood has always been positive.

About ten hours after the lumbar puncture, occipital headache developed, which persisted up to the time of the patient's admission to Bellevue Hospital on January 22. He vomited three days after the lumbar puncture but had no fever. On January 17 he reported back to the west side social hygiene clinic of the department of health, complaining of double vision. A diagnosis was made of paralysis of the left sixth cranial (abducens) nerve.

Examination on admission to Bellevue Hospital showed the pupils to be equal and regular, reacting to light and in accommodation. The patient was unable to move either eye in a lateral direction. The fundi were normal. There was slight weakness of the right side of the face. Neurologic examination otherwise gave normal results.

Lumbar puncture in July 1937 showed a 1 plus reaction for globulin, a 1 plus Wassermann reaction and a normal colloidal gold curve. The cell count was not recorded. Lumbar puncture on Jan 9, 1940 showed a 1 plus reaction for globulin, a 2 plus Wassermann reaction and a normal colloidal gold curve, but the cell count was not recorded. Cisternal puncture on January 23 showed a normal colloidal gold curve, no cells, a negative Pandy reaction and the following Wassermann reactions: with 1 cc of serum, 4 plus, with 0.5 cc, 4 plus, and with 0.1 cc, plus-minus. The Wassermann reaction of the blood on January 23 was plus-minus with cholesterol antigen and negative with alcoholic antigen.

Treatment has consisted of injections of lipobismol, twice a week. The patient has had two injections to date. Since admission to the hospital the paralysis of the right abducens nerve has improved considerably.

DISCUSSION

DR LEO SPIEGEL: This case is most unusual. One sees paralysis of the sixth nerve on one side but rarely bilateral paralysis. The sixth nerve is more frequently injured than other cranial nerves because of its long intracranial course and also because it is exposed and unprotected owing to probable anatomic anomalies. In fracture of the base of the skull this nerve is frequently involved. Paralysis often takes place when the intracranial pressure is altered, as after lumbar puncture. This is given as one of the major causes of paralysis of the sixth nerve. Some observers are unable to attribute it to a definite cause, others believe it is of toxic origin and that in cases of cerebrospinal syphilis it is inadvisable to use lumbar anesthesia, as it predisposes to paralysis of the sixth nerve. In most of the cases reported the condition has followed spinal anesthesia. In this patient the pupils react both to light and in accommodation. This is unusual, as frequently there is a contraction of the pupil because some of the sympathetic fibers to the radiating muscle of the iris pass along this nerve.

DR A BENSON CANNON: Was any local anesthetic used in doing the lumbar puncture?

DR LEO SPIEGEL: I do not know whether a local anesthetic was used or not.

DR E WILLIAM ABRAMOWITZ: Was the facial nerve involved too? The history mentions some facial weakness.

DR ALFRED KESTENBAUM (by invitation): Paresis of the abducens nerve following lumbar puncture is a definite syndrome and is well known. Curiously, it is found almost only in the Italian literature. In the German and the English literature one finds few cases of this sort. The reason for this, I believe, is more a matter of attention paid to this syndrome than the fact that the syndrome is found especially in Italian patients. (The patient presented here is an Italian.) Five to fourteen days after the lumbar puncture there is a sudden appearance of paresis of the abducens nerve. It is mostly unilateral. I found in the literature only 1 case of bilaterality. The presented case would be the second one. All the cases have a good prognosis. In most of the cases the condition occurs after lumbar anesthesia, but in some it is also found after lumbar puncture without anesthesia. I have encountered about 7 cases of this syndrome. There were different causes. In 1 case it occurred after anesthesia in a gynecologic case, in another it followed childbirth, in another it followed surgical treatment, and in at least 2 or 3 it followed lumbar puncture without anesthesia in the treatment of neurologic disease. The frequency of the syndrome is small. In about 20,000 neurologic cases in which I had to give ophthalmologic examinations I noted only 7 cases of this syndrome. That is not even 1 out of 2,000. In the literature are found reports of paresis of the abducens nerve in 1 out of 200 or 300 cases of lumbar puncture, but I think the incidence is exaggerated.

SOCIETY TRANSACTIONS

The cause of this syndrome is not clear. That it is toxic cannot be true, because there have been cases in which anesthesia was not used and because the syndrome does not occur until five to fourteen days after the lumbar puncture. The latter fact is also against the theory of hemorrhage as a cause. The explanation that the paresis of the abducens nerve is due to the original disease, as in this case to syphilis, and that the lumbar puncture only precipitates it is not sufficient, because this syndrome has been found in non-neurologic cases too. In the literature there are still other explanations. Some of these are hypertension in the brain which develops after lumbar puncture, serous meningitis and neuritis of the sixth nerve, but the real cause, the certain cause, of this paresis is not known.

The case presented tonight has two special features. First, the condition is bilateral; secondly, the paralysis was almost complete. That means the motility was almost entirely gone. In the other cases there was mainly moderate paresis only, not complete paralysis.

DR. A. BENSON CANNON: I am inclined to agree with the neurologist, that this patient's paralysis of the sixth nerve is independent of the lumbar puncture and due either to syphilis or to a local anesthetic. In the many thousands of lumbar punctures that I have performed in the last twenty-five years, I cannot recall having had a serious complication. I consider lumbar puncture the most fool-proof method of obtaining spinal fluid. Dr. Verne told me that he had performed 36,000 lumbar punctures on ambulatory patients in clinics in France, without a single accident.

A number of years ago, when I was injecting procaine hydrochloride into the skin and subcutaneous parts of a patient preparatory to performing a lumbar puncture, I noticed the patient breathing with difficulty; repeated convulsions followed for the next twenty-four hours. Had I performed the lumbar puncture, that would have been suspected as the cause of the convulsions. The patient had paralysis of the sixth nerve and partial paralysis of the eighth nerve. The lumbar puncture was finally done a week later, without trouble.

DR. BERNHARD DATTFNER (by invitation): I should like to stress the point that this condition cannot be explained by only one cause. It is generally known that there are many cases in which severe headaches and nausea, often lasting for fourteen days, develop after simple lumbar puncture. The second point is that paralysis of the abducens nerve is common with different conditions. It occurs with diabetes, with increased intracranial pressure, with infections of different kinds, with trauma to the head, with leukemia and with syphilis. It is therefore not surprising that it may be caused once in a while by syphilitic involvement of the central nervous system. The point is, however, that the syndrome is seen much more often following spinal anesthesia than following simple lumbar puncture, and this proves that a toxic factor may play a role in the involvement of this nerve. It is known that when a lumbar puncture is performed the headache is not so severe if the patient is kept in the horizontal position and that it is worse if the patient gets up and walks around. That shows that the hydrodynamic factor plays a role. When all these facts are put together, there is a final point in the anatomic structure mentioned by Dr. Spiegel. The abducens nerve passes through a canal, described in 1906 by Dorello; it is a very small canal, narrow and short. It may happen that in these cases in which paralysis of this nerve occurs a structural anomaly of this canal is concerned. It could explain the fact that in the Italian literature more reports of this syndrome are found. A racial anomaly in the skull may be the cause.

As to the cause in this case, I doubt that syphilis has anything to do with the involvement of the sixth nerve. The patient was well when he went to have the lumbar puncture. He had practically normal spinal fluid, if the Wassermann reaction, which was not strongly positive, is disregarded. The last examination of spinal fluid (cisternal puncture) following the reaction showed it to be normal. There were no cells in the spinal fluid. If this condition were syphilitic meningitis, one would expect to find at least some cells. Therefore, I should say that the

patient perhaps had some constitutional predilection for this condition. It may be that his skull is primarily responsible for the bilateral involvement of both nerves. May I add that the unilateral involvement most often reported may be explained, perhaps, by the fact that the skull is not symmetric, just as the face is also not symmetric? Another point is that this man is very sensitive. After the first lumbar puncture he was sick for four days. That this sensitivity plays a role is proved by the fact that he became sick about ten hours after the puncture and was continuously sick until the bilateral paralysis of the abducens nerve developed. He vomited on the third day, and the paralysis occurred on the seventh day, so the sickness undoubtedly had something to do with the lumbar puncture. There is also the possibility, which has been mentioned by French authors, of a virus infection superimposed on mechanical irritation. In 1937 a case of this kind was cited (Barraux, A, and Bordes, L. A. *Rev. d'oto-neuro-ophth* 15 58, 1937).

DR LEO SPIEGEL. In answer to Dr Abramowitz, the facial weakness was doubtful.

Lichen-Planus-Like Recurrent Syphiloderm with Severe Itching Presented by DR NATHAN SOBEL

V H, a Negress aged 32, is presented from the central Harlem social hygiene clinic of the department of health. In October 1937 the patient had an eruption on the face. The Wassermann reaction of the blood was found to be 4 plus at that time. She was treated at the clinic from November 1937 to June 1939 and received about thirty injections of an arsenical compound and forty injections of a bismuth compound. After the third injection of neoarsphenamine, she states, an eruption appeared on the left elbow and on the right knee. This resisted treatment but eventually cleared up completely, with the exception of a small pea-sized lesion on the right knee. During 1939 the patient received about ten injections of an arsenical compound and five injections of a bismuth compound from June to August, given by her private physician. She also received local treatment with ultraviolet radiation. She had no treatment from the end of August until Jan 16, 1940. In October 1939 the Wassermann reaction of the blood was negative. About September 1939 the persisting pea-sized area on the right knee began to enlarge, and it has reached its present size since November. The patient complained of severe itching, and she applied petrolatum with phenol and acetylsalicylic acid.

When the patient was seen on Jan 16, 1940, she presented a palm-sized plaque on the outer side of the right knee, which was serpiginous in outline, with numerous discrete bluish red nodules the size of a large pea. Extensive pigmentation and accentuation of cutaneous markings were noted within the border. Several discrete nodules were seen outside of the border. There was a similar area the size of a quarter on the left knee. One nodule the size of a large pea was noted on the right arm.

The histologic diagnosis, from a section taken at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, was reported by Dr David L. Satenstein as secondary syphilis. The Wassermann reaction of the blood on January 24 was 4 plus.

Since January 16 the patient has received five injections of a bismuth compound, with substantial improvement in the cutaneous lesions.

DISCUSSION

DR NATHAN SOBEL. I want to point out that when this patient was first seen, about six weeks ago, some of the physicians thought these lesions were lichen planus, even though they were a little larger than the usual lichen planus papules. They were flat and had more of the color of lichen planus at that time than they have now. The serpiginous border of the area favored the diagnosis of syphiloderm.

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DR. LOUIS CHARGIN: This condition appears to be late secondary syphiloderm in a patient who was inadequately treated. The unilaterality, the more or less segmented outline of the eruption and the fact that the beginning lesion is evidently a papule are in favor of a diagnosis of syphilis. This is also supported by the positive Wassermann reaction and by the good response to antisyphilitic therapy. Itching is not especially rare in syphilis of Negroes and especially when local medication has been used, as in this case. The syphilis is not of the follicular type.

DR. NATHAN SOBEL: The interesting feature in this case is the itching. Usually in differential diagnosis if there is a history of itching, syphilis is apt to be excluded, but occasionally, as Dr. Chargin has pointed out, there is a definite history of severe itching. This itching occurred before the patient applied any local treatment. She still has a great deal of itching. There is also one area of involvement on the left knee and another on the right arm. As far as the question of treatment is concerned, she was definitely resistant to treatment, because it took more than one year of treatment to clear up the original cutaneous lesions, one papule remaining on the right knee. Then the lesions began to enlarge again, and she is beginning now to respond again to therapy. One lesion lasted from the time she was previously treated and is only now beginning to heal. This case illustrates the facts that some syphilitic patients require more treatment and a longer course of treatment than are usually advised.

Arsenical Dermatitis. Monorecidive, Followed by Arsenical Dermatitis. Syphilitic Onychia Due to Arsenic? Presented by DR. LEO SPIEGEL.

M. R., an unmarried man aged 46, a sewing machine operator, came under observation and treatment for acute syphilis on Jan. 5, 1935. The Wassermann reaction of the blood was 3 plus with alcoholic antigen and 4 plus with cholesterolized antigen. The slide flocculation test of Kline also gave a 4 plus reaction with both diagnostic and exclusion antigens. He received twelve intravenous injections of silver arsphenamine, totaling 2.3 Gm., at five day intervals from January 7 to February 11. After the last injection arsenical dermatitis developed. He refused hospitalization at the beginning of his illness but finally consented, and he was admitted to Bellevue Hospital on March 1 and was discharged on March 15. The Wassermann reaction of the blood on February 27 was negative with both alcoholic and cholesterolized antigens, and the slide flocculation test of Kline gave a 2 plus reaction with both diagnostic and exclusion antigens.

The patient disappeared from observation and was not seen again until Oct. 2, 1939. He requested treatment for a vesicular dermatitis of the hands. The Wassermann reaction of the blood on the day of his return was negative with both alcoholic and cholesterolized antigens; the slide flocculation test of Kline gave a 2 plus reaction with both diagnostic and exclusion antigens. The examination of the spinal fluid showed that it was normal in all factors.

Since his treatment for syphilis had been inadequate, a course of intramuscular injections of a bismuth compound was advised. He received his first injection on October 2 but failed to report for his second injection until October 19. Subsequent injections were given on November 2, 9 and 16. After the injection of November 16, he failed to report for his treatment until December 5. He then complained of a penile sore, which had been present for about two or three weeks, and stated that he had had sexual intercourse a number of times during the past two months. There was no palpable inguinal adenopathy. The sore was on the shaft of the penis and the location corresponded approximately to that of the previous lesion, when he first came to the clinic on Jan. 5, 1935. Dark field examination showed numerous spirochetes (*Spirochaeta pallida*). Thereupon he received an intravenous injection of 0.04 Gm. of mapharsen. Within four to five hours after the injection he complained of fever and an eruption. The dermatitis was severe and required three weeks' rest before he was able to resume his work. Since December 26 the intramuscular injection of a bismuth compound at four day

intervals has been the only therapy. The Wassermann reaction of the blood on Feb 2, 1940 was negative with both alcoholic and cholesterolized antigens, the Kline flocculation test, however, gave a 4 plus reaction with both diagnostic and exclusion antigens.

For the past two weeks the nails of all the fingers have been exfoliating. New nail plates are growing from the nail root and wall, forcing the old nail plates anteriorly. There is also a dark violaceous or blue line behind the free border of the older nail plates in the nails of some fingers, which Milian has described (Milian, G. Lilac Arch on Nails in Syphilis, *Médecine* 4 112 [Nov] 1922).

DISCUSSION

DR E WILLIAM ABRAMOWITZ. The patient presents a symmetric semilunar groove involving all the finger nails. This has developed in the past two weeks. Do the members feel that this condition is syphilitic onychia?

DR LOUIS CHARGIN. I do not think there is any suggestion of syphilis of the nails in this case. I should rather attribute the dystrophy to a disturbance in the bed of the nail following the arsphenamine dermatitis. An important point to bear in mind is that when a patient becomes sensitive to the organic arsenicals, that sensitivity may remain for a long time, and even a preparation like mapharsen, which rarely causes a generalized dermatitis, may cause a recurrence of the dermatitis. Patch tests before the injection may at times serve to determine whether the patient is still sensitive. In view of the fact that the patient showed the presence of spirochetes in the lesion, arsenic was indicated, but a much smaller dose should have been tried first.

DR LEWIS B ROBINSON (by invitation). I should advise not only being cautious but not giving the patient any arsenic at all. I do not think it makes any difference what dose is given. In these cases in which there has been an arsenical dermatitis, there will be another recurrence if an arsenical is given again.

DR LOUIS CHARGIN. I must disagree with Dr Robinson on this point. I do not think the rule is invariable. One must remember that this patient had an active lesion with spirochetes and therefore arsenic was indicated. If he were a syphilitic patient without active lesions, arsenic would not be indicated, considering his prior dermatitis. I think the arsenic should have been given in this case, but cautiously and in small doses.

DR LEWIS B ROBINSON (by invitation). I still disagree. Giving arsenic means taking a chance, even if the dermatitis occurs in only 1 case out of 10. There are other methods of treatment that can be used.

DR HENRY D NILES. Because of the active lesion containing spirochetes, I believe that there was certainly a justification for giving an arsenical compound to this patient. He reminds me of a patient I had a few years ago who was unable to tolerate even the smallest dose of arsphenamine, neoarsphenamine or silver arsphenamine but to whom I was able to give four full courses of mapharsen in the regular dosage without his having any reaction. I think that even with a history of a previous arsenical dermatitis, some other arsenical, especially mapharsen, was indicated in the present case. I agree with Dr Chargin that the dose could have been much smaller. I do not believe one can assume that because the patient had a dermatitis before he would have one again with mapharsen later. I consider that the question of what to do with him now is the most pertinent one. He will probably have to get along with a bismuth compound and potassium iodide, and one must abandon the administration of arsenicals entirely. Serologically, he has apparently done well with the bismuth compound alone.

DR FRANK E CROSS (by invitation). Sometimes a reaction is favorable, as far as the patient's syphilis is concerned. In some patients who have had only a few intravenous injections of arsphenamine, a high temperature or perhaps some other reaction, develops, and the Wassermann reaction becomes permanently negative without any further treatment, all of which is probably due to a nonspecific fever therapy effect. I think the condition of the nails in this case has nothing

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to do with syphilis but is due to the exfoliative dermatitis. If a patient has a reaction like jaundice or dermatitis, especially if he has it a long time ago, and particularly if the patient contracts syphilis so that he needs an arsenical, I should try an arsenical carefully. This patient received silver arsphenamine, which is usually tolerated well, and although he had a reaction the first time, I think Dr. Spiegel was justified in using another well tolerated drug, like mapharsen, instead. If I had been treating this patient, I would have started with a smaller dose, not more than 0.02 Gm. for the first dose. I would rather divide the dose of 0.04 Gm. and give him a dose of 0.02 Gm. twice a week, proceeding carefully and seeing the patient every time he came in for treatment rather than ordering a course of treatments and seeing him at the end of the course. All patients with syphilis should get individual attention.

DR. LEO SPIEGEL: Regarding the administration of mapharsen to this man, I thought that after a lapse of over four years it was justifiable—in view of the infectious nature of his lesions—to give an arsenical and that mapharsen was chosen because of its supposedly less toxic reaction. The dose of 0.04 Gm. was not considered too high, as the patient weighed over 200 pounds (90 Kg.). No patch test was made, not only because of the long lapse in treatment—with the belief that the sensitivity to the arsenical had by this time disappeared—but also because I have little faith in tests of this kind in determining arsenical sensitivity. The condition of the nails is definitely not syphilitic onychia; nor am I certain that it is the end result of his exfoliating dermatitis.

DR. E. WILLIAM ABRAMOWITZ: Patch tests have not been of much benefit. If the patient gives a positive reaction, an arsenical dermatitis may not develop; if he gives a negative reaction, a dermatitis may still develop. As a rule, however, if the patch test gives a positive reaction, one had better be careful about giving arsenicals.

CLEVELAND DERMATOLOGICAL SOCIETY

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Feb. 22, 1940

Erythroplasia of the Penis. Presented by DR. OTTO E. L. SCHMIDT.

M. D., aged 69, complained of a lesion of the penis of two and one-half years' duration. At the beginning he noticed a grayish, scaly, wartlike lesion on the dorsal surface of the glans, which was tender and which had a red, raw-appearing, nonbleeding surface beneath. The lesion slowly enlarged peripherally and was red, scaling and sharply circumscribed. Three roentgen ray treatments were given by his physician, and three specimens of tissue were removed for biopsy.

Examination reveals a well developed and well nourished man. The glans and the distal half of the penis are covered by a sharply circumscribed, dull red, scaling plaque. The edges of the prepuce are fused to the coronal sulcus in nearly the whole circumference. On the dorsum of the glans there is an area of infiltration about 1 cm. in diameter.

Serologic tests for syphilis gave negative results.

Examination of tissue histologically revealed the skin to be without sebaceous glands, hair follicles or sweat glands. It was covered by stratified squamous epithelium, which in a few small areas showed hyperkeratosis. For the most part the horny layer was absent, and there was mild parakeratosis. The stratum

granulosum was absent, and the rete pegs were wide, long and branched. The papillae of the connective tissue were long and narrow, some extending almost to the surface. The upper portion of the dermis was infiltrated with numerous cells, mostly lymphocytes and occasional large mononuclear cells. Some of the infiltrating cells have extended into the epithelium. There was no evidence of dyskeratosis.

DISCUSSION

DR H. A. HAYNES JR., Akron, Ohio. I suggest the possibility of psoriasis.

DR H. G. MISKJIAN. This man has consulted me in the past, first in April 1939. At that time he had the same lesions as today, and in addition he had a small, round, slightly indurated area on the dorsum of the glans. With the possibility of erythroplasia in mind, I thought of malignant degeneration. I took this area out with a biopsy punch. On examination I was not much surprised to find malignant degeneration with some whorl formation, which suggested prickle cell carcinoma. The rest of the lesion was not indurated and clinically did not correspond to my conception of erythroplasia. I was hopeful that I had taken all the indurated tissue and that induration might not recur, but months later I saw that a new area of induration had developed at that site, and I referred him to the outpatient department of Lakeside Hospital for further study and treatment. On the right side I had taken another biopsy specimen from the red, nonindurated area. There were elongation of the interpapillary pegs and a round cell infiltration. The condition looked more or less like psoriasis, but I do not think it is psoriasis. The case was unusual in my experience. At Lakeside Hospital it was pointed out that on the right side was a small infiltrated area, and a biopsy specimen was taken from there. This section is characterized by enormous elongation of the interpapillary pegs. On the surface of the epidermis there is some parakeratosis. Clinically the condition does not correspond to leukoplakia. Histologically, if the conception of Civatte is accepted, erythroplasia is nothing but Bowen's disease of the membranes. There is nothing to remind one of Bowen's disease in this case, and the condition could not then be erythroplasia. However, Darier stated that erythroplasia is variable and that all examples are not of the same type. I call attention to the elongation of the interpapillary pegs, to the thinning of the epidermis and to the absence of dyskeratosis in the sections. The histologic picture would be more in keeping with a diagnosis of erythroplasia. The section taken from the indurated nodule I think is definitely carcinomatous or precancerous.

DR H. N. COLE. I saw one section from this patient earlier, and I had been told that a diagnosis had been made of erythroplasia. I examined the patient at the same time and called the condition psoriasis. I looked at the section today, and I do not think there is any question about the malignant character of the lesion. Not only is there infiltration down to the corium with islands of the same type, but it is an extreme cellular infiltrate. Considering the patient's age and all other factors, I advise removal of the penis.

DR H. G. MISKJIAN. I did not like to break the news to him myself.

DR HUGO HECHT (by invitation). The first section clinically is psoriasis, but the second one is kraurosis penis. Many years ago I encountered one of the first examples of kraurosis penis. It was similar to this.

DR H. G. MISKJIAN. It is true there is a rare form of kraurosis and that might fit in, but there is no true atrophy here.

DR HUGO HECHT (by invitation). In psoriasis there is parakeratosis, but that is not typical in the section I examined.

Dermatitis Due to Oil of Cinnamon Presented by DR CLYDE L. CUMMER

R. C., a man aged 41, showed swelling of the fingers, with an erythematous-vascular eruption and some fissuring in the interdigital spaces of the left hand. He was seen first in October 1939, and it was suspected that an external irritant was responsible, but it was not until a month later that it was found that just

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prior to the appearance of the eruption, he had started using teal as a dentifrice. He held his toothbrush in his left palm and dropped the teal onto it, the excess running off and through the fingers to the dorsum of the hand. There had been no irritation of the mouth, lips or face at any time. The dermatitis cleared up promptly as soon as the use of the dentifrice was discontinued.

The manufacturers kindly sent specimens of the ingredients of the dentifrice for patch tests. Teal itself gave a strongly positive reaction, as did specimens of the flavoring material, while all other ingredients gave negative results. Samples of the six oils used in blending the flavor were employed for patch tests in 1 per cent solution or in suspension in 50 per cent alcohol. All these oils gave negative results except oil of spearmint, which elicited a slight reaction, and oil of cinnamon, which caused a strongly positive reaction.

DISCUSSION

DR. H. N. COLE: It has been shown that in many cases of so-called bakers' dermatitis the offending agent is cinnamon. If the baker stays away from cinnamon, he is able to carry on his work.

DR. CLYDE CUMMER: Cinnamon is used in the manufacture of some types of hard candy, and candy manufacturers are also liable to have this difficulty. Tulipan (ARCH. DERMAT. & SYPH. 25:921-923 [May] 1932) stated that no instance could be found in the literature up to that date of a dermatitis due to cinnamon. He reported on a baker with severe dermatitis of the hands who had handled cinnamon sugar, a mixture of cane sugar and cinnamon powder.

DR. H. A. HAYNES JR., Akron, Ohio: I have had a patient with a sensitivity to lip stick. Edema of the face developed, but with no involvement of the lips. Patch tests on the skin gave positive results. I cannot explain it, but the lips were not sensitive.

DR. R. E. BARNEY: I should like to congratulate Dr. Cummer on bringing to our attention this new possible source of contact dermatitis.

Papulonecrotic Tuberculid. Presented by DR. CHARLES G. LARocco and DR. CLYDE L. CUMMER.

B. H., a woman aged 37, shows on the arms, especially on the extensor surfaces, extending to the shoulders and to a lesser extent on the chest, numerous small, flat, circular, nonpigmented scars. There are scattered papular and umbilicated papulopustular lesions of rice grain size, some showing necrotic central plugs. These lesions have been appearing since 1923. On the right side of the neck are several irregularly stellate scars, apparently from broken-down tuberculous glands. The glandular condition started when she was 2 years old.

She has received several courses of intramuscular injections of bismuth sub-salicylate, one course of intravenous injections of nearsphenamine and ten injections of gold sodium thiosulfate. She stated the belief that the condition has improved with this treatment.

Fluoroscopic examination of the chest on July 15, 1937 showed no evidence of pulmonary tuberculosis. Numerous serologic tests for syphilis have given mostly negative results, although occasionally there have been slightly positive results. The spinal fluid was normal.

Histologic examination of tissue from one of the necrotic lesions showed the epithelium in most areas to be intact, but there was one area of ulceration which was covered with a thick layer of desquamated epithelium and polymorphonuclear leukocytes. There was an area of necrosis at the site of this ulcer, extending into the corium, and this area showed considerable leukocytic infiltration. The surrounding subepithelial tissue showed lymphocytic infiltration, with a definite tendency toward perivascular distribution. In addition to the ulcer described, there was one area showing moderate hyperkeratosis and some hyaline degeneration of the dermis.

DISCUSSION

DR CLYDE L CUMMER The histologic section in this case was rather unusual. The changes were largely vascular and perivascular. I should like Dr Rehbock, the hospital pathologist, to discuss it.

DR D J REHBOCK (by invitation) I think there was nothing in the section characteristic of tuberculous inflammation. The inflammation was severe, and the cellular infiltrate was extensive, but I could not make any positive diagnosis on the basis of the section.

Vitiligo Presented by DR CLYDE L CUMMER and DR CHARLES G LARocco

C R, a man aged 84, was a uniformly colored, light-skinned mulatto until he was 38 years old. He then noted an itching spot on the forehead, which turned lighter in color, and during the next fifteen years his color turned a uniform white.

He first came to the dermatologic clinic at Charity Hospital on July 19, 1929, because on the ears and the temples "blotches" of returning pigment were noted. He has made occasional visits, the last on Aug 25, 1939, with the same complaint, but it will be noted that at present the entire cutaneous surface is practically free of pigment.

Serologic tests for syphilis on Aug 2, 1929 gave negative results.

DISCUSSION

DR CLYDE L CUMMER This case was presented simply as a matter of curiosity, to show the large extent and the long duration of the trouble.

DR H J PARKHURST, Toledo, Ohio I was surprised to find that the patient has never suffered from sunburn since he has had this condition.

DR CLYDE L CUMMER When the pigment returns, the first evidence is a red spot which fades out and becomes brown.

Tuberculosis Verrucosa Cutis of More Than Sixty Years' Duration Presented by DR CHARLES G LARocco and DR CLYDE L CUMMER

F, a man aged 79, presents an eruption of almost the entire surface of the left buttock, a large part of which is an atrophic white scar. However, within this scarred area are elevated lesions of bright red, with ulcerated and crusted surfaces. At one pole of the scar there is a bright red, crescentic elevated patch about 1 by 4 inches (2.5 by 10 cm), with a verrucous surface.

Serologic tests for syphilis gave negative results.

Histologic examination showed the surface epithelium to be thickened and irregular, with acanthosis and hyperkeratosis. The subepithelial tissues, including the cutis and some of the subcutaneous fibroadipose tissue, showed a severe degree of granulomatous inflammation characterized by scattered small areas suggestive of tubercles, with endothelial cell proliferation and occasional Langhans giant cells. All of the tissue showed extensive infiltration by lymphocytes and numerous plasma cells, and in several areas there was abscess formation, with dense polymorphonuclear leukocytic infiltration. Ziehl-Neelsen and Gram stains showed no evidence of tuberculous or other organisms. The histologic picture was most suggestive of either tuberculosis or syphilis.

DISCUSSION

DR H J PARKHURST, Toledo, Ohio I believe this lesion probably originated around a discharging anorectal fistula.

DR R E BARNEY I had that same impression, and in examining the right buttock just to the right of the anal cleft one sees a depressed scar that might be a healed fistula. I agree with the diagnosis as presented.

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DR. H. N. COLE: I believe this would be a suitable case for treatment by injections of starch, as recommended by Kile (ARCH. DERMAT. & SYPH. 39:471 [March] 1939).

Radiodermatitis with Epitheliomas. Presented by DR. CHARLES G. LAROCCO.

W. T. M., a woman aged 48, had received roentgenotherapy for acne of the face twenty-five years ago.

The forehead, all of the face and portions of the anterior part of the neck present large areas of atrophy and telangiectasia, characteristic of radiodermatitis. In addition, on the right temple there is a warty growth, rounded, well raised and crusted, measuring 5 mm. in diameter. On the left cheek, adjacent to the ear there is a flat, scaly lesion, measuring 7 mm., with a threadlike pearly border. About the eyelids are rice grain-sized to split pea-sized keratoses, suspiciously malignant in appearance.

DISCUSSION

DR. JOHN A. GAMMEL: Despite the fact that these epitheliomas were caused by roentgen rays, I believe they could be attacked therapeutically by a heavy dose of roentgen rays.

DR. CLYDE L. CUMMER: I have recently had a patient with extensive radiodermatitis of the neck of many years' standing. At the suggestion of Dr. Duffy, of the Memorial Hospital in New York, I administered liver extract and vitamin B₁ (thiamine hydrochloride). I do not understand the rationale, but there was considerable softening of the tissues. She looks much better and feels much more comfortable.

DR. EARL W. NETHERTON: There is another treatment that is comparatively new, which I have had occasion to observe in 2 cases. That is the use of petrolatum impregnated with radon. In 1 case roentgen ray dermatitis was on the hands of a dentist, and in the other the condition followed roentgenotherapy of pruritus ani. Improvement has been noted in the relief of subjective symptoms and also has resulted in improving the texture of the skin.

Tumor of Adrenal Cortex, with Subsequent Juvenile Acne Vulgaris, Hirsutism and Precocity. Presented by DR. HAL ELSON FREEMAN.

S. L. F., a girl aged 3 years and 9 months, has had progressive enlargement of the clitoris and labia since the age of 2 months and pubic hair since the age of 7 months. She began talking at 13 months, and the voice became coarse a month later. An acneform eruption developed when she was 19 months old, and when she was 3 years old it spread from the forehead to the nose, face, back and shoulders.

Several immediate ancestors have died from "cancer" in the first decades of life, and several others have had various types of functional endocrine ulcers, in childhood, and there have been several instances of functional endocrine disturbances. The mother has exophthalmos and a palpable thyroid.

Physical examination reveals exceptionally well developed and masculine-appearing legs, thighs and shoulders. The patient is inquisitive and is mentally precocious. The forehead, face, shoulders and back are the sites of pinhead-sized to BB shot-sized follicular, papular and pustular lesions. The affected skin appears oily, and there are many scattered comedos. There is present on the extremities, in the axillas and around the areolas of the breasts abnormally well developed, extensive, dark hair. In the pubic area the hair is exceptionally long and black and is of the adult type. Its distribution, however, is more of the masculine type. The hair of the scalp is of fine texture and lusterless.

The blood pressure has varied between 110 to 125 mm. of mercury systolic and 70 to 85 diastolic. The breasts are not enlarged. There is a firm, painless mass about the size of a medium-sized orange easily palpable in the left upper quadrant of the abdomen. The external genitalia are erythematous and hypertrophic. The clitoris is about 1.375 cm. in diameter and about 3.5 cm. in length when flaccid. The urethra is under this organ, not in it. No prostatic tissue is palpable rectally.

One specimen of urine showed a trace of albumin and another one a 1 plus reaction for sugar, but other specimens have been normal except for the presence of many phosphate crystals and bacteria. Serologic tests for syphilis gave negative results.

The fasting blood sugar on Feb. 14, 1940 was 72 mg and on February 20 104 mg per hundred cubic centimeters. The total chlorides (whole blood) amounted to 184 mg and the urea nitrogen to 11.2 mg per hundred cubic centimeters of blood. Chlorides as sodium chlorides amounted to 304 mg and the calcium content of the blood was 12.6 mg per hundred cubic centimeters. On February 14 the cholesterol content of the serum was 142 mg, and on February 20, 156 mg, per hundred cubic centimeters of serum.

Roentgenograms revealed a normal sella turcica. The epiphyses of the long bones were all present, and all eight of the carpal bones were well formed. Thus,



Fig. 1—Juvenile acne in a girl aged 3 years associated with tumor of the adrenal cortex.

according to Todd's standards, represented a bone age of $10\frac{1}{2}$ to 11 years. A flat roentgenogram of the abdomen and intravenous pyelograms revealed a right kidney with three normal-appearing calices. The left kidney was poorly visualized except for the mass above, which was well outlined, measured 7 by 8 cm and had displaced the left kidney downward considerably.

DISCUSSION

DR. HAL ELSON FREEMAN: This patient is interesting to the endocrinologist, because of the glandular disorder, and to the dermatologist, because of the acne and hirsutism. I have checked up on the cholesterol content of the blood, which should give some evidence of thyroid activity. If there is hypercholesteremia, the basal metabolic rate is low, and if there is a low cholesterol content, the basal

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metabolic rate is high. The blood cholesterol has been in the lower limits of normal. That makes me think that the thyroid function is probably normal. There are several articles in the literature reporting on large series of young girls with acne vulgaris in whom estrogen was absent. Further studies are being made. I anticipate the finding of an increase in androgenic substances, which would explain the presence of the patient's acne vulgaris. Surgical removal of the adrenal tumor is contemplated in the near future.

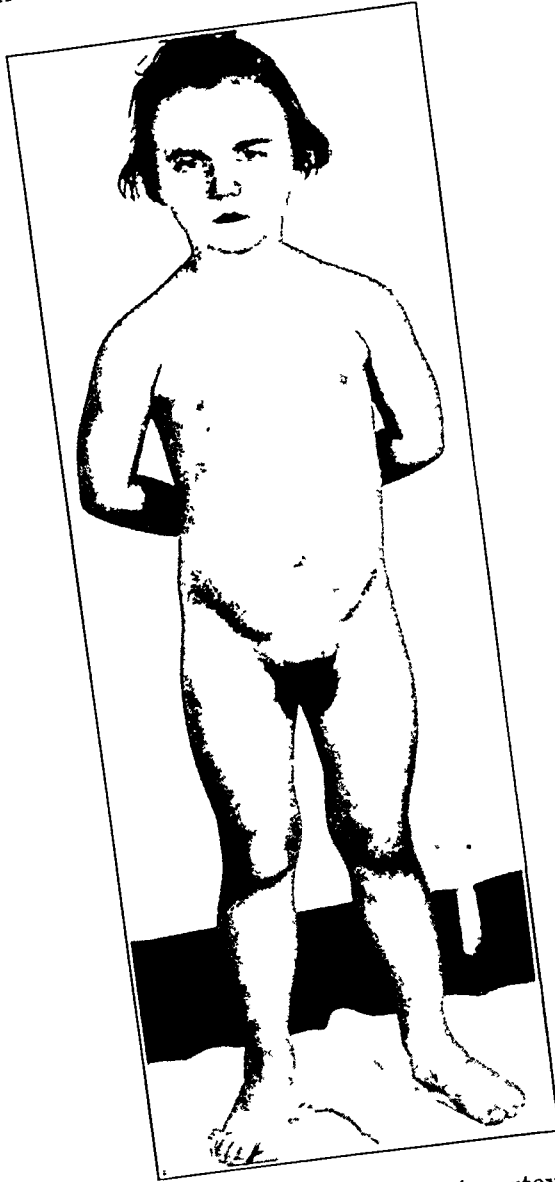


Fig. 2.—Hirsutism due to tumor of the adrenal cortex in a girl aged 3 years.

NOTE.—Her intelligence quotient was found to be 124. On March 20 the urinary assay showed 148 international units of androgen and 20 rat units of estrogen per twenty-four hour output. Preoperatively, desoxycorticosterone was administered. The sodium and potassium content of the blood and the blood and serum chlorides were followed carefully both preoperatively and postoperatively.

Surgical operation for removal of the adrenal tumor was performed on April 16. The tumor was friable grossly and was composed microscopically entirely of immature cells of neoplastic type, which were called carcinoma solidum by members of the department of pathology, City Hospital.

On the fifth postoperative day the patient died from the effects of a streptococcal septicemia and pleuritis. The blood pressure had been maintained at satisfactory level before this complication developed.

There were small areas of metastases in the lungs. The right adrenal was normal at autopsy.

Pseudoxanthoma Elasticum Presented by DR JOSEPH H SHEPARD (by invitation)

R S, a woman aged 31, had been troubled with a slowly progressing eruption since childhood. At present she is five months pregnant (her first pregnancy). She stated the belief that during the second and third months of her pregnancy the involved areas increased in size more rapidly than ever before but that no progress has stopped completely.

The patient's sister, aged 31, has the same condition, of about ten years' duration, in the same locations and in addition behind the knees. However, none of the patches were as prominent as in the patient. The patient's sister has 2 children, aged 11 and 9 years, who now have no evidence of this trouble. The patient's brother, aged 24, has had the same condition on his neck for two or three years but it has not become prominent.

There are rather sharply defined areas covering the front and sides of her neck, the flexor folds of her arms and the upper inner surfaces of her thighs. The areas are composed in general of indefinite, pinhead-sized to pea-sized, firm, flesh-colored papules, which in places have coalesced to form much larger patches. In places there are fine streaks 0.5 to 1.5 cm in length. The papules, patches and streaks are all definitely yellowish. In areas around her neck there are many telangiectatic blood vessels. She has no history of any ocular trouble. The light and accommodation reflexes were normal. The tension was normal. Ophthalmic examination revealed several spots of choroiditis with pigment disturbance in both eyes. Examination of the right eye disclosed many angioid streaks beginning from a circular area around the disk and extending like wagon wheel spokes toward the periphery of the fundus. The maculas seemed normal, but there was one angioid streak close below the macula of the left eye, as well as a few other angioid streaks.

Serologic tests for syphilis gave negative results. The hemogram was normal. Histologic examination revealed clumps of degenerated and swollen elastic tissue in the middle and lower parts of the cutis. Except for this finding the tissue was essentially normal.

DISCUSSION

DR H N COLE: This patient presents the most extensive example of pseudoxanthoma elasticum I have ever seen. The familial character of the disease has been shown, and I wish to congratulate Dr. Shepard on the excellent presentation.

DR JOSEPH H SHEPARD (by invitation): I shall attempt to follow this family over an extended period in order to see if this disease develops in the children, the sister and the child of the patient.

DR C J SHEPARD, Columbus, Ohio: The lesions on the elbows develop following pregnancy. What connection her pregnancy has had, I do not know.

A Case for Diagnosis (Syphilitic Dactylitis?) Presented by DR CLYDE CUMMER and DR CHARLES G LAROCCH

J B, a Negro aged 56, while on duty as a railroad porter, on Jan. 6, 1919, injured the tip of the left index finger while he was tucking bedding under a berth. There was no pain until two days later, when the finger became swollen. When seen by us twenty-three days after the injury, the finger was swollen to twice its normal size, the skin was red and glossy, the markings were obliterated and the paronychia was badly swollen. While the appearance suggested the presence of a pyogenic infection, the attending surgeon had incised it on two occasions and found none.

The patient stated that he had a penile sore thirty years ago. Mercury pills were taken for six months, but no subsequent treatment was received. The pupils were irregular in outline and fixed to light. The knee jerks were active. The Wassermann and Kline reactions of the blood on January 31 were positive.

Since January 28 the patient has received three injections of bismuth subsalicylate intramuscularly and iodides by mouth. Soon after treatment was started the pain abated and the swelling subsided greatly. The patient was able to return to work on February 10.

A roentgenogram taken on January 10, four days after the injury, showed a comminuted fracture of the base of the distal phalanx, involving the joint. The position was good. Some hypertrophic changes in the bone were noted along the shaft of the proximal and middle phalanges of the fingers.

A second roentgenogram, taken on January 19, showed decrease in the density of the distal phalanx, so that the bone detail was poorly defined. There was also decreased density of the middle phalanx, especially in the region of the head.

A third roentgenogram, taken on February 15, forty days after the injury, showed considerable deformity of the base of the distal phalanx. The fragments were in apposition, with little displacement. There was no evidence of callus. Some absorption of the fragments was observed. The joint space between the middle and the distal phalanx was poorly defined as a result of atrophy or absorption of the joint cartilage. As compared with the second roentgenogram, this one showed more decalcification of the middle and distal phalanges and some absorption of the fragments of the distal phalanx.

DISCUSSION

DR. I. L. SCHONBERG: In view of the history of injury, I offer a diagnosis of a possible paronychia due either to a staphylococcus or to a fungus.

DR. CLYDE L. CUMMER: We presented this case with the idea of getting the opinion of the members as to whether the changes in the bone are due to trauma or in part to a latent syphilitic infection. The first roentgenogram taken after the injury showed merely a fracture. The patient had no pain in the finger until two days after the injury, at which time the finger became swollen. The attending surgeon thought there might be some infection, as Dr. Schonberg has suggested, and made an incision, but no pus was obtained. The second roentgenogram showed decalcification of the middle phalanx. The attending surgeon felt that the old syphilitic infection could account for it. The attending roentgenologist was in doubt. Immediately after administration of iodides and bismuth there was a decided improvement in the finger. The swelling went down at once, and the patient was willing to return to work. I can hardly accept Dr. Schonberg's suggestion after seeing the improvement. The most recent roentgenogram made a few days ago showed decalcification with no callus formation.

DR. JAMES R. DRIVER: I was interested in the roentgenograms of the finger. The first one did not show osteoporosis. The bone looked approximately normal. From the photographs it seems as if some secondary infection was present. It is known that infections in the finger, particularly in the distal phalanx, will produce this type of reaction in the bone. The fact that it did not show in the first roentgenogram would lead me to believe that the osseous changes were not due to syphilis but to secondary infection. However, syphilis may be a factor in the prolonged healing.

DR. C. GLENN BARBER (by invitation): I looked at this patient from the orthopedic standpoint. I did not feel after looking at the roentgenograms that one could attribute the changes shown by them to anything other than trauma. However, examination of the man leaves no question that there is something in addition to the trauma. He had rather extensive involvement of the soft parts. One function of a joint is motion and the other is stability. He had decided limitation of motion. He had comparatively painless instability of his joint. Whether

the condition happens to be of the Charcot type or some other form of syphilitic involvement, the joints are less painful than with ordinary forms of injury

DR H N COLE I think this patient is a good illustration of the influence of trauma on an old syphilitic infection. It is well known that as the result of trauma a syphilitic process may flare up

Tertiary Syphilis (Gummas of the Arm) Presented by DR CLYDE L CUMMER and DR CHARLES G LAROCO

B L C, a man aged 34, presented himself first at the outpatient department of Charity Hospital with many irregularly circular and stellate depressed white scars on the right arm, beginning about 3 or 4 inches (7.5 or 10 cm) above the wrist and extending almost to the axilla. They were most closely grouped over the extensor surface around the elbow, and interspersed were a few nodules and occasionally irregular, deep, discharging ulcers. The scar tissue had caused considerable contraction of the soft tissues. The arm was held in an extended position, and flexion was possible only through an angle of about 15 or 20 degrees.

The patient stated that these sores started appearing at least ten years ago, breaking down and healing and followed by others. The only treatment employed had been salves.

The Wassermann and Kline tests gave positive reactions. Roentgenologic examination showed a slight irregularity of the periosteum of the distal end of the humerus, principally along its epicondylar line, and slight subarticular demineralization of the lateral aspects of the humerus and radius at the humeroradial joint. The irregularity of the soft tissue was shown, and it would appear that the lesions of the bone and joint were simply secondary to the lesion of the soft tissue.

DISCUSSION

DR R E BARNEY The process has almost healed with the exception of two areas. One of these is below the left elbow. I think with any lesion that has been present for this length of time, one should consider the possibility of malignant degeneration.

DR C GLENN BARBER (by invitation) The cutaneous condition has improved considerably. A more judicious time for taking a specimen of tissue for biopsy would be at some later stage.

DR CLYDE L CUMMER I felt that since the patient has had no treatment whatever, trauma from biopsy might make the whole condition break down. The biopsy can be postponed and performed if the lesion does not improve.

A Case for Diagnosis (Trophic Elbow Joint Due to Syringomyelia? Tertiary Syphilis with Charcot Joint?) Presented by DR CLYDE L CUMMER and DR CHARLES G LAROCO

M B, a Negress aged 41, presented a greatly swollen and deformed left elbow joint. Increasing swelling had been noted for the last two or three years, and this finally made the patient think the joint had been dislocated. There was relatively little pain on motion, although there has been more in the last few months. The arm showed several superficial atrophic scars, said to have resulted from burns.

The patient had been seen in the dermatologic clinic of Charity Hospital in 1934, at which time the Wassermann reaction of the blood was strongly positive. At this time a diagnosis of latent syphilis was made, and three courses of injections of a bismuth compound and two courses of neoarsphenamine had been given.

Neurologic examination revealed the loss of the sensation of pain and temperature in both upper extremities, the vibratory sensation of the upper left extremity and of both lower extremities, and the sense of discrimination of the upper left extremity. The pupils reacted to light. The consensual reaction was present. The reflexes of the knees were equal and active. The reflexes of the

ankles were equal and active as well. The Romberg test gave a positive result. The spinal fluid on Oct. 25, 1939 was normal.

A roentgenogram of the left elbow showed the presence of innumerable large and small calcified bodies within the joint and periarticular joint spaces or bursae, the largest being 3 cm. in diameter. There was almost complete loss of the humero-ulnar joint space. There was no evidence of old fracture.

DISCUSSION

DR. H. N. COLE: I regard this case as an extreme example of Charcot joint of the elbow. There is bony proliferation and along with it fluid in the joint. It is true that one may have such involvement with syringomyelia as well as with tabes. Examination of the spinal fluid gave negative results, but with old syphilis the spinal fluid may sometimes show nothing.

DR. I. L. SCHONBERG: I should like to know why the temperature of the affected arm is higher than that of the opposite arm. Has aspiration been performed?

DR. C. GLENN BARBER (by invitation): The elbow was aspirated, but no fluid was obtained. I think this condition is a typical Charcot joint. The patient does not show decided manifestation of tabes, but that is not necessary. Many patients before showing any neurologic signs will show pronounced changes in the joints. She shows characteristics of a lessened normal function. Her flexion is greatly limited. Supination and pronation are limited. She now is beginning to show lateral instability. She can completely dislocate her elbow and put it back. I think the present symptoms are due to particles of bone acting as foreign bodies. If it is thought necessary, these can be removed.

A Case for Diagnosis (Tuberculosis of the Elbow Joint? Tertiary Syphilis of the Elbow Joint?). Presented by DR. CLYDE L. CUMMER and DR. CHARLES G. LAROCO.

G. P., a Negro aged 33, came to the orthopedic clinic of Charity Hospital on Oct. 24, 1939, stating that five days previously, while working in an automobile junk yard pounding with a heavy hammer to smash old cars, his right arm suddenly became sore and his hand swollen. The elbow has been painful since this time.

Crepitation and fluctuation were noted. The joint was aspirated at that time, and no fluid was secured. Later a history was obtained of soreness of the elbow for a year prior to the time when the acute symptoms appeared.

The right elbow is bent at an angle of about 160 degrees. Flexion and extension are practically impossible. There is swelling of the joint and obvious deformity, with the appearance suggesting that the forearm has been pulled up behind and above the end of the humerus so as to shorten the arm. Crepitus is present.

Roentgenologic examination showed destructive arthritis, the destructive process involving all of the joint surfaces of the component bones, the outlines of which were irregular. There were no evidences of hypertrophic changes, but multiple loose bony particles were seen within the joint, probably sequestrums from destroyed bone ends. The capsule of the joint appeared distended.

A history was obtained of a penile lesion seventeen years previously. No anti-syphilitic treatment had been received. The Wassermann and Kline tests gave positive reactions on Oct. 28, 1939. The spinal fluid was normal on February 15.

On February 14 the elbow joint was opened to obtain material for biopsy. The capsule was much thickened and gelatinous but free from fluid.

Histologic sections of the soft tissue showed all but one of the fragments to be composed of a loose type of connective tissue, which was moderately well vascularized and showed a few small areas of lymphocytic infiltration. One fragment was composed of fibrous connective tissue and voluntary muscle, and in the central portion of the tissue there were two focal areas of inflammation, which were highly suggestive of miliary tubercles. They were characterized by small

amounts of necrosis, with surrounding epithelioid cell formation and associated Langhans giant cells. No other similar lesions were found in any of the other fragments of tissue.

Sections of the fragment of bone showed one surface to be a periosteal surface which presented no significant pathologic change. No articular cartilaginous tissue was seen. The bony trabeculae showed no significant change, and there was no significant change in the fatty marrow. A diagnosis of chronic inflammation of the synovia and adjacent fibromuscular tissue, probably tuberculous, was made.

DISCUSSION

DR H. H. JOHNSON JR. I had an almost identical case at Lakeside Hospital with a rather rapidly progressing process in the elbow joint. The patient was treated for syphilis. In the meantime the joint was aspirated and guinea pig inoculations made, and the condition was proved to be tuberculous. Have such inoculations been made with aspirated material from this patient?

DR C. GLENN BARBER (by invitation). Since no fluid was obtained by aspiration, guinea pig inoculations were not made.

DR EARL W. NETHERTON. Since this man has lost 25 to 30 pounds (11 to 13.5 Kg.) and has frequent night sweats, I should like to ask the presenters if a roentgenogram of his chest has been made.

DR CLYDE L. CUMMER. I do not believe that as yet roentgenographic examination of his chest has been done. The man slipped entirely away from observation, and a social service worker contacted him and brought him in for this meeting.

Keloidal Scars at Sites of Bullae from Barbiturate Poisoning Presented by DR CLYDE L. CUMMER and DR CHARLES G. LA ROCCH

D. A., a man 21, was admitted to Charity Hospital on July 2, 1939, in coma. He had taken 150 grams (9.7 Gm.) of phenobarbital thirty-six hours previously in a suicidal attempt. At examination on admission the temperature was 40.6 C (105.1 F), the respirations, 60 per minute, the pulse rate, 160, and the blood pressure, 126 mm of mercury systolic and 40 mm diastolic. The skin was livid, and there was cyanosis, but no cutaneous lesions were seen. Signs of pneumonic consolidation were found at the bases of both lungs. All reflexes, including the corneal, were absent.

At first sulphydryde was given through a stomach tube. Eighteen hours after admission, when it was discovered that phenobarbital had been taken, picROTOXIN was administered.

Ulcerations over the sacrum were observed on the fourth hospital day, and hemorrhagic bullae were noted on the heels. These lesions eventually broke down and were not completely healed until six weeks later.

Two weeks after admission there were signs of peripheral neuritis, with paralysis of the right ulnar nerve.

Now the patient presents keloidal scars on pressure points on the sacrum, the tips of the heels and the outer malleoli, at the sites of healed ulceration.

Urinalysis showed no abnormalities. Leukocytes in the blood varied from 7,900 to 26,500 per cubic millimeter. Diplococci were found in the sputum but could not be typed.

DISCUSSION

DR CLYDE L. CUMMER. I should like to have you call on Dr. Miller, of the resident staff of the hospital, who has observed a number of cases of this kind in the emergency service at the hospital.

DR ROBERT C. MILLER (by invitation). Since the first of July 5 patients with severe barbiturate poisoning (doses of from 60 grains [4 Gm.] of sodium amytal to 250 grains [16 Gm.] of barbiturate having been taken in attempted suicides) have entered the hospital. On 4 of the 5 hemorrhagic bullae were observed, which appeared from the second to the fifth day after the barbiturate had been taken.

Picrotoxin was used in various doses (from $\frac{1}{2}$ grain to 2 grains [0.02 to 0.13 Gm.]) over twenty-four to thirty-six hours. Four of the patients recovered.

DR. CHARLES G. LAROCO: Dr. Cummer and I have been especially interested in this group of cases because of the development of hemorrhagic bullae. I have never seen the barbiturates produce lesions of this type when given in therapeutic doses. We wondered whether the picrotoxin was a factor in producing this. I believe this substance is analogous to metrazol, and there are no reports of any cutaneous eruption following therapy with that drug. We are inclined to believe that this cutaneous manifestation is a result of barbiturates.

DR. CLYDE L. CUMMER: The conditions in these cases were all due to suicidal attempts. There is supposed to be a close margin between the therapeutic and toxic dose of picrotoxin. Persons who have had these large doses of barbiturates will take more picrotoxin than can be given to a person in health. The question arose in our minds as to whether the bullae were from the picrotoxin or from the barbiturates. There are several cases of barbiturate poisoning reported in the literature; hemorrhagic bullae apparently developed in all of them, and the patients all went through the same stage of prolonged ulceration.

ATLANTIC DERMATOLOGIC CONFERENCE

New York, March 9, 1940

DR. FRANK C. COMBES and DR. GEORGE C. ANDREWS, *Presidents*

DR. J. GARDNER HOPKINS and DR. ANTHONY C. CIPOLLARO, *Secretaries*

Trophic Ulcer of the Nose. Presented by DR. MAURICE J. COSTELLO, New York.

H. A., an American aged 47, a watchman, was first seen in November 1938, referred from the Manhattan Eye, Ear and Throat Hospital. He gave a history of sudden loss of speech and of sensation in the left side of his body several days before a diagnostic spinal puncture was performed. He stated that an ulcer appeared on the left side of his nose the following day. While in the hospital he complained of excessive sweating limited to the left half of his body. He had had a severe injury of the head twelve years before, accompanied by transitory hemiplegia on the left. The duration of his complaint is eighteen months.

Examination shows an ulcerating lesion of the left nostril with some destruction of the ala nasi. He also has a proliferative ulcerating lesion on the septum resulting in occlusion of the left nostril. There is beginning atrophy of the septal cartilage. In an area extending about 1 inch (2.5 cm.) around the left nasal aperture there appears to be an infectious eczematoïd dermatitis. The sinuses appear hazy on transillumination. There is moderate injection of the blood vessels of the scleras.

Physical examination showed the heart to be slightly enlarged to the left. There was some tenderness in the left upper quadrant of the abdomen. Neurologic examination showed generalized hyperreflexia, with bilateral Hoffmann signs and equivocal Babinski signs. There was a transitory ankle clonus on the right. No evidence of thrombosis was noted.

On Feb. 2, 1939 the nasal discharge showed no tubercle or lepra bacilli. Culture of the material showed *Staphylococcus aureus*, a few hemolytic streptococci and *Micrococcus catarrhalis*. The Wassermann and Kahn reactions were negative on five occasions. Blood counts were normal except for mild leukocytosis. The urine was normal.

On Nov 25, 1938 histologic examination showed papillary hyperplasia of the stratified squamous epithelium, hyperkeratosis, a small area of ulceration and an acute inflammatory reaction. In the submucosa there was dense connective tissue, with considerable inflammatory reaction. Histologic diagnosis was hyperkeratotic papilloma.

The patient received antisyphilitic therapy, including neoarsphenamine and saturated solution of potassium iodide. The treatment had no effect on the lesion.

Leukemia of the Skin (Aleukemia) Presented by DR E WILLIAM ABRAMOWITZ, New York

J L., a Russian man aged 69, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. The eruption on the back was noted about the summer of 1939. It became generalized, finally involving the face, trunk and extremities. When the patient first presented himself there were pea-sized to olive-sized, raised, purplish, hard nodular lesions, particularly on the back. He complained of itching, but there was no pain. Erythematous nodular lesions of moderate size were also present on the face, the eyebrows and the upper and lower extremities. His general health has been good.

The Wassermann and Kahn reactions were negative. The urine was normal. A blood count on admission showed 108 per cent hemoglobin and 5,200,000 erythrocytes per cubic millimeter, a differential count showed 64 per cent polymorphonuclear leukocytes, 19 per cent lymphocytes, 6 per cent eosinophils, 3 per cent basophils and 8 per cent monocytes. The color index was 1 and the red cells were normal. At present the blood count has shown a slight drop in the leukocyte count. The only other change is that there is slight macrocytosis. Since the patient has been receiving injections of liver his leukocyte count has risen from 3,000 per cubic millimeter to normal. Histologic examination showed perivascular infiltration composed almost entirely of small round cells of the small lymphocyte type. There were a few wandering connective tissue cells. The histologic diagnosis was lymphatic leukemia of the skin.

The patient is receiving filtered roentgen rays to the affected areas. He has also been receiving increasing doses of liver by injection.

DISCUSSION

DR J FRANK FRASER, New York. The condition in Dr Abramowitz' case is a typical example of the aleukemic form of lymphatic leukemia. Probably leukemia cutis of the lymphoid variety always occurs in the aleukemic form. Too many clinicians overlook the fact that the fundamental changes in leukemia are in the tissues and not in the blood. In the great majority of cases, as in the case under discussion, the initial lesion is in the lymph nodes. In a case reported (Rossie, R., cited by Richter, M. M., in Downey, H. *Handbook of Hematology*, New York, Paul B Hoeber, Inc., 1938, vol 4, pp 2887-3028) the skin seemed to be the primary site of the disease, as the lymph nodes were not enlarged. The blood picture is secondary and a manifestation of metastasis.

In regard to the histologic picture, the infiltration of neoplastic cells may be (1) diffuse, (2) periglandular or (3) perivascular. The sections in the case under discussion show a perivascular distribution.

In the case which follows this one, presented by Dr Traub, there is a note on the pathologic report that the microscopic picture is suggestive of both lymphatic leukemia and lymphosarcoma. This is not surprising, for it is impossible at times to differentiate these two conditions on histologic grounds. The trend among present day investigators seems to lend strong support to the view that lymphatic leukemia and lymphosarcoma are the same disease, the only difference being that in lymphatic leukemia there is metastasis to the blood stream.

In regard to treatment, the plan followed at the Memorial Hospital is to place the patient in the Hubble chamber. In this chamber the patient receives

70 r per hour for twenty out of twenty-four hours. This method is efficient in reducing the blood count, though it may cause anemia. I understand that in the present case Dr. Abramowitz is using the spray method. Theoretically this method should lessen the chances for metastasis.

DR. E. WILLIAM ABRAMOWITZ, New York: After the first few roentgen ray treatments, the patient showed a distinct drop in the leukocyte count, from 8,000 or 9,000 to 3,000 per cubic millimeter. He was getting about one-half erythema dose with filters, and I had to cut down the dose and increase the intervals between treatments. He was also given liver extract. The lesions responded beautifully. As you see today, most of them are now nothing but pigmented lesions. I think Dr. Fraser is correct. This man's condition probably started with glandular enlargement, and the cutaneous condition, I believe, appeared later. Examination of the cells obtained by sternal puncture showed that they were practically normal in every way.

Lymphatic Leukemia. Presented by DR. EUGENE F. TRAUB, New York.

E. D., a housewife aged 64, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, where she has been under observation since Sept. 15, 1939. There have been a loss of weight and a tired feeling. General physical examination showed little lymphadenopathy, most prominent in the groin and axillas. Her previous history was irrelevant. The duration of the eruption is ten to twelve months.

An eruption has been present mostly on the face, the extensor aspects of the arms and hands and the back, with occasional scattered lesions elsewhere on the body and legs. These lesions as well as the lymphadenopathy have responded quickly to roentgenotherapy, and many of the lesions have now disappeared. The original appearance was that of erythema multiforme of an iris type. More recently only bullous lesions have been noted, particularly on the arms. The lesions are bright red raised wheals varying in size. Some are excoriated and some papular and vesicular, suggesting papulovesicular urticaria. On the dorsa of the hands and fingers she has had, at times, hemorrhagic lesions, some of which have been slightly ulcerated. She also has an ulcerated lesion on the labium majus.

Examination of the blood gave the following results:

Date	Erythrocytes per Cubic Millimeter	Leukocytes per Cubic Millimeter	Hemo- globin, per Cent	Polymorpho- nuclear		Lympho- cytes, per Cent	Mono- cytes, per Cent	Eosino- phils, per Cent
				Leuko- cytes, per Cent				
10/14/39	4,380,000	29,100	78	4		95	1	..
10/26/39	4,070,000	12,200	82	10		89
11/ 2/39	3,640,000	6,700	74	10		88	1	1
1/22/40	3,740,000	7,350	79	36		58	5	..

Histologic examination of an excised lymph node showed that the normal architecture of the node was no longer present; there was uniform architecture everywhere, with lymphoid elements extending into the capsule and surrounding fat. There was a relatively uniform distribution of lymphoid cells, the nuclei of which had distinct membranes and within which there were prominent chromatin masses. Here and there enlarged reticulum cells were seen. Mature lymphocytes formed the minor proportion of the cells. The small blood vessels were uniformly engorged. The histologic diagnosis was lymphatic leukemia of the lymph nodes, with a note that the histologic picture was one that was suggestive of both lymphatic leukemia and lymphosarcoma. The blood examination, however, favored the former diagnosis (20,000 leukocytes per cubic millimeter, with 90 per cent lymphoid cells).

Histologic examination of the lesion on the vulva showed cutaneous and subcutaneous tissue, the surface of which was stratified squamous epithelium with a

few hair follicles. It was not ulcerated. Immediately beneath this and extending for some distance into the subjacent connective tissue there was a rather diffuse cellular reaction. In some areas the cells of this reaction were mainly lymphocytes, often accompanied by hypertrophy of reticulum cells. In other areas there were plasma cells or eosinophils or an admixture of both. The eosinophils, however, were usually in small numbers. In a few places the cells were nearly all plasma cells. The examination showed leukemic infiltration of the cutis and chronic inflammation of the cutis. There was a note that it was rather difficult to determine how much of this infiltration was leukemic and how much was due to chronic inflammation. The admixture of plasma cells and eosinophils was probably not a part of the leukemic process. The histologist was inclined to interpret the plasma cells and eosinophils in the specimen as due to inflammation.

DISCUSSION

DR EUGENE F. TRAUB, New York. Unfortunately there were few lesions present for inspection today. The patient originally came in with what looked like erythema multiforme, and then an intensely itching vesiculobullous eruption developed which might have been mistaken for erythema multiforme or dermatitis herpetiformis. Such conditions have been previously reported. The roentgenotherapy she has received to the lymph nodes and to the skin has caused most of the lesions to disappear. The treatment was discontinued shortly before this meeting, but there is only one bullous lesion present on the arm today. One lesion showed leukemic infiltration, so I think in this particular patient the lesions of the skin were actual leukemic lesions and not leukemids.

Scleroderma Over the Right Pectoralis Muscle, Associated with Calcification of the Right Subdeltoid Bursa. Presented by DR. JOSEPH J. ELLER, New York

L. B., an American saleswoman aged 43, one year ago had pain over the right subdeltoid bursa. A roentgenogram showed complete calcification. She received diathermy treatments. A roentgenogram of the bursa at the present time is normal. Five months ago she noticed a painless, whitish, hardened and thickened area of skin over the right pectoral muscle extending to the anterior axillary line. This area has gradually enlarged. When she was 2 years old a gland was removed from the right side of her neck, but the diagnosis is unknown. For several years the patient has been under an emotional strain due to financial reverses.

Examination shows a widely thickened plaque about $3\frac{1}{2}$ inches (9 cm.) in diameter extending from the anterior aspect of the chest to the anterior axillary line. The skin is fixed to the underlying tissue. In the right axilla there are two small pea-sized movable tender nodes. The patient complains of intense pain in the right shoulder when the arm is moved in certain directions.

Chemical examination of the blood showed 117 mg. calcium and 34 mg. phosphorus per hundred cubic centimeters of blood. Urinalysis showed many epithelial cells, many mucous threads and a few leukocytes (probably contamination from vaginal secretions). A blood count showed 4,420,000 erythrocytes and 8,200 leukocytes per cubic millimeter and 75 per cent hemoglobin, with 6 per cent eosinophils. The basal metabolic rate was $+6$ per cent.

Histologic examination (Dr. David L. Satenstein and Dr. Wilbert Sachs) showed the collagen bundles of the middle and upper parts of the cutis to be greatly condensed and arranged as a compact layer of bundles parallel to the surface. The elastic tissue was present throughout and similarly arranged as the collagen bundles. In part the elastic fibers were somewhat fragmented.

Radiation from a thin window lamp (Westinghouse) was used locally in erythema doses weekly. Thyroid extract was given orally, $\frac{1}{8}$ grain (75 mg.) twice a day. The patient has been under treatment for the past four weeks, and the patch of scleroderma has become softer and thinner.

Amelanotic Melanoma. Presented by DR. FRANK C. COMBES, New York.
R. S., an Austrian Jewess aged 50, a housewife, was previously presented at a meeting of the New York Academy of Medicine, Section of Dermatology and Syphilology, on Jan. 2, 1940, for diagnosis (ARCH. DERMAT. & SYPH. 42:175 [July] 1940).

The patient has had an eruption for seven months on the lower third of the right leg. It began as a half lentil-sized, brownish lesion which slowly enlarged. Three months after its onset, pinhead-sized, flesh-colored, elevated, semisolid satellites appeared within several inches of the first nodule. The lesions are for the most part discrete. A few have coalesced and become pigmented. Later the color deepens so that the mature lesions become bluish black. The visible metastases of the skin now number about sixty, being all below, lateral and medial to the original lesion from which a biopsy specimen was taken. There are no other lesions on the body. The right inguinal lymph nodes are palpable but not visibly enlarged.

A roentgenogram of the chest showed no metastases. Histologic examination showed the upper third of the cutis, immediately beneath the epidermis, to be replaced by neoplastic cells arranged in solid sheets and clusters. Some of the cells were large and round; others were cubical, and some were spindle formed or three cornered. They contained large, pale nuclei. These were starlike cells with dendrites. Between these cells were a few spindle cells containing brown pigment. The main cells themselves did not contain pigment or mitotic figures. At one point there was an invasive projection of cells and some invasion of the lymphocytes. The histologic diagnosis was malignant melanoma (nonpigmented). Treatment has consisted of 15,000 milligram hours of radium therapy to the affected areas. The lesions have flattened somewhat.

DISCUSSION

DR. GEORGE C. ANDREWS, New York: I should like to ask whether pigment appeared in the lesions only after they had been irradiated. I had a case of amelanotic melanoma on the chin which after deep roentgenotherapy became heavily pigmented. Sometimes metastases from a pigmented melanoma do not show pigment clinically, and sometimes the metastases from a nonpigmented melanoma show pigment clinically. There seems to be no rule about it, but it does happen that pigment sometimes develops after roentgenotherapy in these lesions.

DR. A. BENSON CANNON, New York: I thought it was the general opinion that radiation was useless in the treatment of melanocarcinomas. The only form of treatment which offers any hope of relief or cure is surgical intervention. I should suggest removal of the extremity and resection of the regional glands.

DR. E. WILLIAM ABRAMOWITZ, New York: Such grave prognoses are always being expressed about these lesions. The other day I saw a woman who had had a melanoma removed from the back fifteen years ago. The lesion was excised widely; the surgical intervention was followed by radium treatment. She has remained well.

DR. JOSEPH J. ELLER, New York: I agree with Dr. Cannon that wide surgical excision is the proper treatment in this case, possibly followed later by irradiation.

DR. GEORGE C. ANDREWS, New York: I feel the same way, that surgical treatment is the only kind for melanoma. The reason the patient I just mentioned was not treated surgically at first was that the lesion was about 1½ inches (3.8 cm.) in diameter and located on the chin, and it would have necessitated an extensive and mutilating operation, which the patient unfortunately had to have anyway. He is now free of the disease. The roentgenotherapy had little beneficial effect on the growth and only made it more difficult to remove later.

DR. FRANK C. COMBES, New York: In answer to Dr. Andrews' first question, when this patient first appeared in the hospital she had about a dozen small

miliary to pinhead-sized nodules. They were flesh colored and glistened like vesicles, so much so that the clinical diagnosis suggested was that of lymphangioma circumscriptum. The diagnosis of melanoma was never entertained until the histologic examination was made. The pigmentation made its appearance long before radiotherapy was instituted. I agree with those who recommend surgical intervention in this case. I am not responsible for the treatment. The patient was transferred to the surgical department, and radiotherapy was recommended by the surgeons. If I recall correctly, she has an enlarged gland in the right groin, which does not improve the prognosis. The report of amelanotic melanoma was made by Dr Symmers' laboratory on the histologic basis. I feel confident that if a biopsy were made now, plenty of melanin would be found in the tissue.

Melanocarcinoma Following the Treatment of a Common Mole Presented by DR MAURICE J COSTELLO, New York

A W, a girl aged 18, was presented at a meeting of the Manhattan Dermatologic Society on Dec 12, 1939 (*ARCH DERMAT & SYPH* 42 162 [July] 1940)

DISCUSSION

DR DAVID BLOOM, New York. I have had the opportunity to observe this case from the beginning. From this and another similar case I have observed, I came to the conclusion that darkly pigmented plaques with downy hair which look infiltrated in the skin and are not well defined raised tumors above the skin should not be exposed to the effect of solid carbon dioxide or electrolysis but should be treated radically or not at all.

DR FRANCIS A ELLIS, Baltimore. I should like to ask Dr Traub's opinion on this case, whether he thinks the growth originally was a common mole or whether it was a "junction type" nevus. Of course as there was no biopsy before it was first treated, I do not see how one can be certain which it was.

DR H FORD ANDERSON, Washington, D C. I think this case should be presented as one of "melanoma in spite of the therapy." I think the condition was probably a melanoma in the beginning, and I do not think the treatment had anything to do with the production of the melanocarcinoma.

DR JOSEPH J ELLER, New York. Surgical intervention must also be recommended in this case as the preferable treatment.

DR MAURICE J COSTELLO, New York. Before treatment this girl was presented at the Wednesday afternoon dermatologic conference at Bellevue Hospital. All present agreed that clinically the lesion was a common pigmented mole. She came to the dermatologic clinic, not because there was any change in the mole but because the lesion was a cosmetic defect of which she was becoming sensitive. It was removed in the manner stated, and the cosmetic result was excellent. A year later the pea-sized, bluish black, solid lesion which she now presents made its appearance. The report of the histologic examination then was a pigmented nevus. Because my clinical impression of the lesion was that of melanoma, I checked the histologic specimen and had two dermatopathologists and two general pathologists examine it. They agreed that it was a melanocarcinoma. I think this young woman presents a melanocarcinoma which followed the treatment of a common mole, as known clinically.

DR EUGENE F TRAUB, New York. This is a most interesting case that must be given serious consideration. The patient was seen by a number of able dermatologists, so that there cannot be much doubt as to the appearance of the original lesion. The unfortunate thing, however, was that no section of the original growth was examined microscopically, and so it must be assumed because of the presence of hairs that this was a common mole or intradermal nevus. While the presence of hairs is usually common with the ordinary mole and rare with a junction type nevus, a number of junction type nevi do show fine downy hairs, such as may still be seen at the margin of this lesion today. There seems

to be little question but that at the present time this patient has a malignant melanoma. According to the classification recently published (Traub, E. F., and Keil, H.: The "Common Mole," *ARCH. DERMAT. & SYPH.* **41**:214 [Feb.] 1940), the fact was stressed that the pure intradermal nevus did not terminate either as a cancer or as a melanoma, so far as could be determined. A mixed type was added, however, because not infrequently combinations of the various varieties were found. For example, one might see an intraepidermal nevus, an intradermal nevus or a junction type or any possible combination of the three. Had an original histologic examination been done in this case, the lesion would in all probability have fallen into this mixed type, because it presented some of the clinical attributes of an intradermal nevus but has terminated as to the junction type nevi. Numerous examples of such combinations have been seen, and if one can find an example, naturally it is reasonable to assume that many others can be brought to light on further search. It is probable that the long-continued treatment given this patient stirred up that portion of this nevus in which the activity was at the epidermodermal junction, with the resultant development of a melanoma. Until there is more definite information about the frequency of occurrence of these mixed types, even the most expert clinical knowledge does not warrant the assumption that one can always be right in clinically labeling a given lesion as a common mole or intradermal nevus. Therefore, I believe that when there is the slightest possible doubt, it is advisable to treat such lesions more radically than was done in this case and not subject the lesion to too much repeated irritation. This is one of several examples that I have now observed in which what appeared to be a benign pigmented nevus, treated with solid carbon dioxide, terminated in a malignant melanoma. Unfortunately in these cases it is generally difficult to find out the exact appearance of the original growth, and there has usually been no histologic examination made at the onset to determine what type the lesion is. I do not wish to leave the impression that all nevi with activity at the epidermodermal junction become malignant melanomas, but it is these lesions which may give rise to such a change.

Chronic Ulcer of the Back. Tumor of the Leg (Syphilis? Dermatitis Artefacta?). Presented by DR. J. GARDNER HOPKINS, New York.

R. S., an American aged 30, a typesetter, was previously presented for Dr. Frank E. Meleney at a meeting of the New York Dermatological Society on Nov. 28, 1939 (*ARCH. DERMAT. & SYPH.* **41**:952 [May] 1940). At that time he presented a huge wedge-shaped ulceration in the interscapular region measuring about 3 inches (7.5 cm.) across and 6 inches (15 cm.) in a vertical direction, the apex extending down to the tips of the spinous processes. It showed no decided improvement until the patient entered the hospital in January 1940. It has now healed, leaving a red contracted scar.

Histologic examination of the ulcer in 1939 showed necrosis and granulation tissue, with numerous giant cells. Tuberculosis or syphilis were considered as possible diagnoses.

The tumor of the right leg was not mentioned at the time of the previous presentation. In December 1939 pain developed along the medial border of the right foot, interfering with his sleep. It was not increased by standing or by pressure. This first called his physician's attention to the condition of the leg. The patient thinks that eight or nine years ago he hurt this leg while playing football and that since then it has been larger and distinctly harder than the left leg. He states it has changed little during this time. For an indefinite time he had noted numbness and paresthesia in the right foot, but he did not call his physician's attention to the leg until the pain developed. The mass in the right leg was explored, and a large mass of inflammatory tissue was found attached to the posterior surface of the interosseous ligament. A large portion of the mass was removed to relieve the pressure on the posterior tibial nerve.

At present there is still a hard mass lying in or beneath the right soleus muscle. There is complete anesthesia of the greater part of the sole and the inner side of the heel, corresponding to the distribution of the cutaneous branches of the posterior tibial nerve. There is paresthesia of the dorsum of the foot.

Wassermann reactions have been repeatedly negative. Roentgenograms of the bones of the right leg are normal.

Histologic examination of the mass removed from the right calf showed at the periphery striated muscle which was intensely involved in an inflammatory process. The central part showed dense collagenous tissue and vascular inflammatory tissue. There was infiltration largely of lymphocytes, with large mononuclear cells. There were many giant cells, some strongly suggestive of Langhans cells and others containing vacuoles and of a foreign body type. There were occasional polymorphonuclear leukocytes and small areas of necrosis. There were pseudotubercles, especially in the neighborhood of the small vessels. No organisms were seen in sections stained with Gram, Ziehl-Neelsen or Levaditi stains. Cultures showed scant growth of staphylococcus in forty-eight hours (not typical of tuberculosis, sarcoid or syphilis).

The ulcer on the back healed under recent treatment with staphylococcus bacteriophage and scarlet red. The patient has been treated for the past four weeks with a bismuth compound, arsphenamine and potassium iodide. The ulcer on the back was nearly healed before this treatment was begun. The mass in the right leg has not changed.

DISCUSSION

DR BERNARD L. KAHN, Philadelphia. I should like to ask Dr Hopkins what type of bacteriophage he used in this particular case. About nine years ago I treated 22 patients with pyoderma with bacteriophage (Kahn, B. L. *Bacteriophage Therapy for Pyoderma*, *ARCH. DERMAT. & SYPH.* 24:218 [Aug.] 1931). With some varieties of bacteriophage (Swan-Myers) good results were obtained, while with others there was failure.

DR DAVID BLOOM, New York. I should like to ask Dr Hopkins how much antisyphilitic treatment the patient has received. I have observed several cases of extensive and deep involvement, as in this case, in which the lesions were definitely gummas. Because of the great amount of necrotic tissue involved, it takes a considerable time to realize the effect of specific therapy.

DR JACOB H. SWARTZ, Boston. I should like to ask whether studies were made for the presence of anaerobic streptococci. In other words, did Dr Hopkins consider the possibility of a symbiotic infection?

DR MAURICE J. COSTELLO, New York. I should like to ask if Dr Hopkins looked for the microaerophilic streptococcus which Dr Meleney has identified as the cause of lesions of this type. If that were found, a lesion of this size would probably not heal without complete surgical excision.

DR R. H. RULISON, New York. I attended the meeting of the New York Dermatological Society at which this case was presented, and the condition has certainly improved since that time. The suggestion was made then that it might be a symbiotic infection. In the history I note that the man has had, on the basis of some such investigation, a staphylococcus bacteriophage which caused almost complete healing of the ulcer.

DR J. GARDNER HOPKINS, New York. First, in regard to the question of anaerobic streptococci, the patient was originally sent to Dr Meleney because of his published descriptions of that type of infection. Dr Meleney thought that clinically the condition was not at all like the disease he has described, for one reason on account of the lack of undermining of the edges. However, he studied it carefully from that standpoint and did not recover anaerobic streptococci. Cultures showed staphylococci which were phage sensitive, and the patient was treated with bacteriophage. It is with that method of treatment that he has shown the greatest improvement. As to specific therapy, the picture is a little confused. After his presentation the patient continued treatment with bacteriophage, with

careful occlusive dressings, and the ulcer almost healed before specific treatment was started. Since that time he has had five injections of old arsphenamine and about ten injections of a bismuth compound. He also received potassium iodide until iododerma developed. The treatment with bismuth and arsphenamine has been continued since he left the hospital, but since his leaving the ulcer has again begun to break down. It appears that the antisyphilitic treatment has had no effect.

Necrobiosis Lipoidica Diabeticorum Without Diabetes. Presented by DR. EUGENE F. TRAUB, New York.

K. C., a woman aged 26, born in the United States, a receptionist, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, with an eruption of two years' duration. There is no history of diabetes or tuberculosis in the patient or in her family. In each instance, after a slight bruise, three areas developed on the left leg, and more recently, also apparently after bruises, several marks have developed on the left leg. The areas begin as inflammatory nodules, with the subsequent development of plaques.

Examination shows shiny yellowish brown or waxy plaques, with telangiectatic vessels at the sites of well developed lesions. Earlier lesions are indicated by inflammatory nodules. About the border there is a violaceous color.

The Wassermann and Kahn reactions were negative. The urine was normal. Chemical examination of the blood showed 65 mg. true dextrose (the normal value being 60 to 80 mg.) per hundred cubic centimeters. A sugar tolerance test showed no sugar in the urine while she was fasting, at the end of the first hour or at the end of the second hour; the values for the blood sugar were respectively 60 mg. during fasting, 65 mg. at the end of the first hour and 50 mg. at the end of the second hour per hundred cubic centimeters. Histologic examination showed a practically normal epidermis. There was swelling of the connective tissue fibers of the middle part of the corium. Between these and extending down to the hypoderm were islands of round cells, endothelial cells and giant cells of the Langerhans type.

Treatment has been symptomatic.

DISCUSSION

DR. FRANCIS A. ELLIS, Baltimore: I disagree with this diagnosis. The case reminds me of one I observed some years ago which I thought was a case of scleroderma-like changes with sarcoid, but the results of biopsy were pathognomonic of granuloma annulare. The patient was not diabetic, and the entire lesion healed with roentgenotherapy. I wish to suggest the diagnosis here of granuloma annulare. I think that the histologic section helped to confirm that diagnosis, while clinically the case is similar to the one I had. Were fat stains made?

DR. WILBERT SACHS, New York: In this section there was no granular degeneration whatever. There was perivascularitis and some swelling of the intima, so much so that the lumen of some vessels was almost entirely obliterated. Of course, with necrobiosis lipoidica one may find tubercle formation in different parts of the cutis. In this particular section there were no tubercles, but there were many giant cells and few or no histiocytes. The lack of histiocytes and lack of granular degeneration in no way give the appearance of granuloma annulare.

DR. JOSEPH C. BERNSTEIN, Baltimore: Some time ago I had occasion to study cases like this, particularly with reference to granuloma annulare (Bernstein, J. C.: *Necrobiosis Lipoidica Diabeticorum* [Urbach]: Comparison with Granuloma Annulare, *ARCH. DERMAT. & SYPH.* 36:282 [Aug.] 1937). There happened to be in the series of patients with granuloma annulare 2 who also had diabetes. I think it is difficult and sometimes impossible to differentiate these two conditions both clinically and histologically. In my study I was fortunate to anticipate the histologic picture and made plans accordingly. In performing the biopsies I made frozen sections first (lipoid stains) to ascertain if the patients with granuloma annulare

and diabetes would show the presence of lipoids between and adjoining the collagen bundles, which is a pathognomonic finding. They failed to show this structure. On the other hand, the patients with true necrobiosis lipoidica diabetorum did show lipoids between the collagen bundles. The type of cellular infiltrate is insignificant, and I do not believe a diagnosis can be made with the routine hematoxylin and eosin stain. Unless lipoid studies are made, it is impossible at times to differentiate the two entities. In this particular case the diagnosis is disputable. In the first instance, the patient does not have diabetes. Secondly, there are many conditions which cause degeneration of the collagen tissues, some of which are inflammatory, and in which one can find the picture which has been presented here today.

DR FRED D WEIDMAN, Philadelphia. I should like to register on the side of the diagnosis as presented. In cases of both granuloma annulare and necrobiosis lipoidica diabetorum, there is necrobiosis. Of course, if one confines oneself to the item of necrobiosis, one is bound to get overlappings between the two diseases. In that dilemma, one can turn to other features, and in this particular case there are giant cells which I think are of the foreign body type. They indicate a reaction against the necrobiotic material, and, as far as I know, such a giant cell reaction against granuloma annulare has not been recorded. The matter of lipoidal degeneration I think is entirely incidental, just as in a tumor one part of the necrotic material may have undergone a further change, namely, fatty degeneration and another part may not have proceeded so far. At this juncture the matter of the arteriosclerosis is an important point. This patient is only 26 years old, but the endarteritis is marked. I do not think that the absence of diabetes should militate against the diagnosis of necrobiosis lipoidica, because, after all, whereas in the original series of cases diabetes might have been associated, there is now a notable accumulation of cases of such a dermatosis in the absence of diabetes. The criticism should lie rather with the original nomenclature, "necrobiosis lipoidica" should not have been saddled down with the necessity of being associated with diabetes. The disease might have been called "necrobiosis lipoidica arteriosclerotica," for example. That would also have included cases in which the arteriosclerosis is not diabetic.

DR J FRANK FRASER, New York. I should like to ask Dr Traub whether the sections were stained with methyl violet.

DR R H RULISON, New York. Merely on clinical grounds today, I think this case is a classic one of necrobiosis lipoidica diabetorum.

DR EUGENE F TRAUB, New York. I should like to call attention to the history of another case. The patient did not come today, but she has an advanced, even ulcerative, example of this disease, with no present evidence of diabetes, though she has a history of diabetes. As all the recent tests show no evidence of diabetes, I should have had to say it was a case of necrobiosis lipoidica diabetorum without diabetes if the diabetes had not been discovered by accident a number of years ago. I believe this is an important point, because undoubtedly some patients who are supposedly not diabetic, if followed long enough, may show sugar and other symptoms of diabetes. In other words, the fact that some of the patients do not have diabetes when they are examined does not exclude the possibility that at some other time in their lives an excessively high sugar concentration may be present. Before attention was drawn to this syndrome, I had 4 cases, 3 of which I presented at various societies with various diagnoses of morphea with a tuberculoid structure or granuloma annulare or some similar diagnosis. I thought, because of both the clinical appearance and the histologic changes, that the condition was in some way related to tuberculosis. After this syndrome was described I reviewed the cases, and I have since made a report on them. They all fit in with necrobiosis lipoidica diabetorum. None of the patients had diabetes, as far as I could discover. I followed some of them for three or four years. Of course, this is in line with Belote's recent article. I had a recent case which I thought might possibly be an example of necrobiosis lipoidica diabetorum, but

it proved to be a case of granuloma annulare. I think this syndrome is not clean-cut or well understood yet, and I expect that perhaps something more may be discovered in the future about it. I suspect some of these conditions may be related to tuberculosis in some way. This patient and the other one who failed to come today were studied, and no evidence of tuberculosis was found in either one. However, I had a case of lupus vulgaris in which extensive grafts of skin were placed over the scalp, which took perfectly, but six months later if that area had been screened off and inspected any one would have seen a typical picture of necrobiosis. I suggest, therefore, that this possible relation to tuberculosis be studied further. In the case under discussion, special stains have been used and were reported by Dr. Barthel as showing characteristic changes seen in this disease. Therefore, there is histologic confirmation of the clinical diagnosis.

Fixed Eruption Due to Mapharsen. Presented by DR. MAURICE J. COSTELLO, New York.

Y. W. T., a Chinese man aged 39, was previously presented from Bellevue Hospital at a meeting of the Manhattan Dermatological Society on Nov. 14, 1939 (ARCH. DERMAT. & SYPH. 41:943 [May] 1940).

DISCUSSION

DR. F. CORMIA, Montreal, Canada: I should like to make a suggestion in regard to treatment in this case. I have 2 similar cases in which the condition was caused by neoarsphenamine and recurred on attempts at subsequent therapy. In both cases I was able to resume the treatment with neoarsphenamine after having first fully saturated the patients with large doses of vitamin C intravenously. Curiously, patch tests in areas of previous dermatitis subsequently gave negative results. I have another case in which there was a previous generalized exfoliative erythroderma from arsenic, with a strongly positive reaction to a patch test. After one week of massive intravenous doses of vitamin C, 1,000 units daily, the reaction to a patch test was negative. I should think that possibly treatment with mapharsen might be resumed in this case following the massive therapy with vitamin C.

DR. E. WILLIAM ABRAMOWITZ, New York: I agree that this condition is a typical fixed eruption from mapharsen. There have been several cases reported. All of the arsenicals used in antisyphilitic therapy have been known to produce this type of eruption. The inorganic compounds like solution of potassium arsenite (Fowler's solution) and other inorganic compounds and some of the less complex organic arsenicals like sodium cacodylate and mercury salicylarsenate (enesol) have not been reported as producing a fixed eruption. Yet I should not be surprised if they would some day. In this case it is interesting that the author tried to show that phenolphthalein was responsible for this eruption. At one time it was said that phenolphthalein was the only drug that could cause this type of fixed eruption. Dr. Louis Chargin has a large series of cases of fixed eruption from the arsenicals. He has had some interesting experiences. He has given some of the patients phenolphthalein, and they have had not only a flare-up in the old patches but new fixed lesions. Those produced with phenolphthalein would flare up only with administration of arsphenamine. I am surprised to hear that one can obtain a positive reaction to patch tests of fixed eruption which belongs to the erythema group. Reactions to this type of fixed eruption may be responsible. Originally, when Naegeli (*Cor.-Bl. f. Schweiz. Aerzte* 47: 1291, 1917) described fixed eruptions from arsphenamine, he said they were not a contraindication to further use of the drug. Epinephrine might prevent their occurrence. I tried it, and it did not work. These eruptions sometimes do not recur, even without anything being done to prevent them.

ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY

A BENSON CANNON, New York I have never regarded a fixed eruption as a contraindication to the further use of arsphenamine, nor have I found it wise to make any alteration in the treatment of syphilitic patients with arsphenamine

MAURICE J COSTELLO, New York Since the last date mentioned in the literature this patient has been given an intravenous injection of 0.3 Gm of arsphenamine, an erythematous halo appeared around the lesion in the axillary space, but similar lesions around the mouth, eyelids and ear were not noticed

Case for Diagnosis (Multiple Recurrent Disseminated Painful Ulcers) Presented by DR JOSEPH J ELLER, New York

JOHN, an American aged 26, states that since 1932 he has had multiple ulcerated and deep subcutaneous abscesses scattered over the trunk, in the axillae, on the forearm and on the legs At times he has had an intermittent high temperature, but for the past four weeks the temperature has been normal The patient has never been well He was a premature infant and had feeding difficulties early in life Boils began to develop when he was 10 months old, and during his childhood he had three hundred and fifty boils Tonsillectomy was performed at the age of 7 At 14 he had a mastoidectomy In 1932, after a severe attack of rheumatic angina, all his teeth were removed The patient had successive crops of abscesses throughout his childhood, but since 1932 they have assumed a different character and behavior His diet has always been limited by his refusal to eat raw fruits or uncooked vegetables The patient's father had generalized eczema and ringworm, especially localized on the hands and feet and involving the nails He also had a toxic adenomatous goiter and died suddenly, apparently of a heart disease

Physical examination shows a large, palm-sized, fairly well demarcated, superficial ulcer scar on the flexor surface of the left arm through which the veins can be seen On the neck there are inflammatory nodes and scars similar to keloid The abdomen is covered with superficial healed scars of various sizes and there are no active lesions present in this area The back shows a similar pattern The left thigh shows large serpiginous ulcerations, with a tendency toward central healing The right leg shows serpiginous plaques with central healing, leaving a shiny atrophic surface Other patches contain discrete reddish nodules There are many intradermal pustules on the lower part of the leg The calf and thigh show a similar involvement The axillae show areas of scarring Axillary and cervical lymph nodes are pea sized, firm, discrete and not adherent to the skin The inguinal lymph nodes are marble sized and somewhat matted together

Wassermann reaction was negative Blood complement fixation tests for syphilis and a blood agglutination test with *Brucella abortus* gave negative results

The urine was normal Repeated blood cultures were negative, and the results of examination of the stool were normal Chemical examination of the urine showed 130 mg of sugar per hundred cubic centimeters Blood counts showed 98 per cent hemoglobin and 4,630,000 erythrocytes per cubic millimeter, at various times showed achromia, anisocytosis and poikilocytosis The leukocyte count was 5,750 per cubic millimeter, with a differential count of 14 per cent polymorphonuclear leukocytes, 71 per cent lymphocytes, 6 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils, all of which were normal in size and appearance The lymphocyte count has varied from time to time from normal to 40 per cent lymphocytes and 6 per cent neutrophils Sternal puncture in 1937 gave a negative (at the time of puncture the count was 75 per cent polymorphonuclear leukocytes, 6 per cent monocytes and 9 per cent lymphocytes) Myelopoiesis showed normal maturation A recent culture of blood taken during removal of a biopsy showed a large amount of pure *Streptococcus haemolyticus* Blood from the vein the next day showed no growth Culture of a portion of

the biopsy specimen showed numerous fungi (the growth in the culture has not yet been classified).

Histologic examination of a specimen of skin showed the surface epithelium thickened in places. The corium showed a great increase in fibrous connective tissue, with areas of granulation tissue within which was a dense infiltration of chronic inflammatory cells. The cells were chiefly mononuclear, and many eosinophils were present. There was evidence of old hemorrhages, the pigment being phagocytosed by macrophages. The histologic diagnosis was chronic granulomatous inflammation of the skin with ulcerations.

Treatment has been varied. The patient received long courses of general irradiation with ultraviolet and roentgen rays to isolated regions. Cod liver oil and viosterol were given by mouth and liver and iron parenterally and orally. Staphylococcus stock vaccines have been administered. He has had numerous local applications, including allantoin. All of these methods were without effect. Sulfanilamide, azosulfamide (neoprontosil, disodium 4-sulfamidophenyl-2'-azo-7'-acetyl-amino-1'-hydroxynaphthalene-3',6'-disulfonate) and sulfapyridine were given a fairly thorough trial over a period of weeks, in small doses. Sulfapyridine seemed to help the lesions slightly. *Brucella abortus* vaccine given in several courses as a therapeutic trial seemed to bring about definite improvement, but this was followed by relapse. Eight small blood transfusions at weekly intervals were followed by the greatest improvement, in that all lesions disappeared from the trunk. However, ulceration on the buttocks and thighs continued without remission. The lesions recently have improved under the following regimen: bed rest, constant nursing care and applications of boric acid ointment. He is now receiving vitamins and brewer's yeast orally and compound solution of iodine U. S. P. intravenously. Since fungi have been found he is receiving 5 per cent aqueous solution of gentian violet to one leg. One area is now under treatment with zinc chloride cream.

DISCUSSION

DR. WILBERT SACHS, New York: This case presents a most unusual clinical picture. According to a slide which I saw a little while ago, throughout the entire cutis there is organizing granulation tissue, and in the deep part of the cutis there is one isolated tubercle. I should of course hesitate to make any diagnosis on the presence of one tubercle or even on one slide, but I think I can rule out syphilis in this case. I suggest the possibility of some form of tuberculosis.

DR. DAVID BLOOM, New York: I suggest the diagnosis of chronic ulcerative pyoderma, a condition which is seen in debilitated patients.

DR. MAX SCHEER, New York: I should like to ask whether any examinations were made for the presence of *Nocardia* or any other of the family of Actinomyces.

DR. LEE MCCARTHY, Washington, D. C.: I had the pleasure of observing a case like this with Dr. Fields several years ago. We were able to rule out amebic parasites and obtained staphylococci and streptococci. The patient's condition cleared up after six months with transfusions and acetarsone by mouth.

DR. JOSEPH J. ELLER, New York: In this case there were a profuse growth of *Str. haemolyticus*, which was not recovered from the blood at any time, and a profuse growth of fungi, which have not been identified when grown on agar. The patient has improved with hospitalization and nursing care. No examination was made for *Nocardia*.

Maduromycosis (Black Grain Variety). Presented by DR. PAUL E. BECHET, New York.

A. N., a man aged 67, born in the United States, is presented from Welfare Hospital, with an eruption of the right hand of seven years' duration. The patient states that he has never been outside of the immediate environs of the city of

New York On Nov 24, 1932 he was admitted to the Neurological Hospital, Welfare Island, suffering from arteriosclerosis, hypertension and cerebral thrombosis, which caused a mild paralysis of the extremities On that day he fell and scraped his right hand along a wooden floor, thereby causing many splinters and particles of dirt to enter the skin of the hand Since that time the swelling of the hand has increased progressively

Examination shows the right hand to be greatly swollen and deformed On the palmar surface, nodules, pustules and many sinus openings can be discerned From these sinuses black grains are discharged of a fish-roe-like appearance. Some of the lesions resemble small cystlike, lentil-sized, violaceous to black spots, others appear pustular with black dots The dorsum of the hand presents many cystlike swellings but no discharging lesions

Direct examination of crushed granules revealed a tangled mass of mycelia which were septate Dr George M Lewis, in whose service the patient was originally, succeeded in cultivating a species of *Hormodendron*, which has not apparently been previously reported in the black grain variety of maduromycosis Further investigation of this fungus and its relation to maduromycosis is under way Repeated roentgenograms of the hand showed no involvement of the bones The Wassermann reaction was negative The results of urinalysis and complete blood count were normal

Histologic examination showed acanthotic epithelium, which contained dense nests of inflammatory exudate with some attempt at nodule formation These inflammatory nests consisted of lymphocytes, plasma cells, histiocytes and small giant cells The giant cells were circular and contained from three to eight nuclei which were evenly dispersed throughout the cytoplasm The periphery of the exudates consisted of collections of xanthoma cells The nests of cells were surrounded by dense connective tissue capsules The connective tissue of the corium was condensed, thickened, hyalinized and irregularly dispersed by the inflammatory exudates There was considerable endarteritis

The patient is taking 390 minims (24 cc) of a saturated solution of potassium iodide daily No signs of iodide intolerance have as yet been noted There has been no gastric upset The patient's digestion is normal and his appetite good There has been a definite improvement since iodide therapy has been instituted

DISCUSSION

DR GEORGE M LEWIS, New York There are two types of lesions The palm shows discharging sinuses, from which dark amorphous-appearing granules could be obtained, and on the dorsum of the hand are discrete, firm, subcutaneous swellings Histologic examination showed black granules in the substance of these lesions on the dorsum of the hand The mycologic study is still in progress The exact classification of the causative fungus is not yet certain, but it has been tentatively classed as *Hormodendron pedrosoi* (Brumpt 1921), which resembles *Phialophora verrucosa*

DR FRED D WEIDMAN, Philadelphia On the whole, clinically this condition resembles more a mycetoma than it does chromomycosis Generally, with chromomycosis there is a verrucous dermatitis However, there is a notable accumulation of cases in which that has not been true, when the disease occurs on the upper extremities, it is not likely to be a verrucous dermatitis Therefore, the way is still open for this condition to be classed as chromomycosis, provided the mycologic examination shows that one of the chromomycotic species is finally determined The "naked eye" appearance of the culture is strikingly like the species of chromomycosis fungus isolated in Texas, *Phialophora verrucosa* I might say, incidentally, that the first case of chromomycosis in the United States was observed by Dr C Guy Lane of Boston and that the original description of *Phialophora verrucosa* came through his efforts The appearance in the sections is not that of chromomycosis The festooned way in which the fungus substance is arranged is like that of maduromycosis, and the "spores" are also more like those of

maduromycosis. The cells in chromomycosis are large, have a double contour and exhibit pseudobudding. Therefore, there is here a conflict between several important items in deciding between mycetoma and chromomycosis, which can scarcely be decided until the identity of the parasite is finally determined.

DR. C. GUY LANE, Boston: Unfortunately I did not happen to observe this particular case. I was interested in the photographs. The palmar lesions show no resemblance and the lesions on the back of the hand show little resemblance to those in the case from which the *Phialophora verrucosa* was cultured originally some years ago. In that case there were three or four lesions alone on the buttocks. In the discharge of one of these lesions there were found some curious organisms. Later a whole lesion was removed, about 1 to 1.5 cm. in diameter, and from that the cultures were obtained. That particular lesion looked more like an early lesion of verrucous tuberculosis. The purplish color with no great amount of pigmentation, perhaps not any more than is met in that particular person, gave that impression. The lesion healed after excision, and there was no recurrence.

Reticuloendotheliosis; Mycosis Fungoides (?). Presented by DR. HERMAN SHARLIT, New York.

M. G., a Polish man aged 50, a blacksmith, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, with an eruption of two years' duration. The eruption involves the entire body except the hands and the penis. It is reticulated, brownish and scaly, with numerous telangiectatic areas. There is decided lichenification, especially of the neck. The mucous membranes are comparatively free. There are many depigmented areas inside reticular lesions. On the neck and elbows there are islands of clear areas. The patient gives no history of ingestion of drugs. Examination of the urine for arsenic gave negative results. The Wassermann and Kahn reactions were negative. The blood count was normal. Histologic examination was reported as "reticuloendotheliosis, and disorganized, and in the upper part of the epidermis was slightly acanthotic and histiocytes was noted. The cells were of different sizes and shapes. A fine reticulum was present as well as pigment.

DISCUSSION

DR. A. BENSON CANNON, New York: I do not know of any condition except lichen planus which will leave such extensive pigmentation, and this patient has innumerable lesions that are characteristic of this disease. I have found closely studded, discrete, flat-topped, violaceous, striated, shiny, pinhead-sized to millet seed-sized papules all over the body and extremities, with some linear lesions. On the elbows and outer surfaces of the arms I noticed a number of annular lesions from 0.5 to 1 cm. in diameter that were in every respect typical of lichen planus. I have never observed an example of mycosis fungoides which even remotely resembled this condition.

DR. WILBERT SACHS, New York: The presence of a fine reticulum and many histiocytes would definitely rule out lichen planus and would be much in favor of the diagnosis as presented.

DR. HERMAN SHARLIT, New York: Naturally the suggested diagnosis of mycosis fungoides in this case could have been based only on the cytologic examination of a section. It would appear evident from the many cases presented here this afternoon with the tentative diagnosis of mycosis fungoides that there is no correlation between clinical pictures and this cytologic diagnosis. It would be well to realize that the diagnosis of mycosis fungoides is always one of cytologic changes, and this cytologic picture evidently occurs frequently in a group of clinical conditions. Only in the unusual instance does this condition in its clinical

evolution lead to tumor formation and death. For this reason the histologic diagnosis of mycosis fungoides can have prognostic significance only in terms of the clinical picture. In my experience, generalized eczema due to external irritants is the most frequent cause of the production of the cytologic picture of mycosis fungoides. In this case I should be inclined clinically to agree with Dr. Cannon, but the histologic picture does not bear out this diagnosis.

A Case for Diagnosis (Pemphigus?) Presented by DR. EUGENE F. TRAUB, New York

I. M., a man aged 46, presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, was presented at a meeting of the New York Dermatological Society in November 1934, in February 1935 (*ARCH. DERMAT. & SYPH.* 32: 978 [Dec.] 1935) and on Oct. 24, 1939 (*ibid.* 41: 788 [April] 1940).

Despite all types of therapy, the disease has been slowly progressive with practically only the slightest of remissions. He still presents numerous irregular, ragged ulcerations on the buccal mucosa, the tongue and the roof of the mouth. Crusted lesions appear on the lip, the nose and about the eyebrows.

DISCUSSION

DR. JOSEPH V. KLAUDER, Philadelphia: I believe this patient has pemphigus of the mucous membranes, including the conjunctiva (ocular pemphigus). This diagnosis can be made definitely if it can be established that the lesions in the mouth are vesicles. He does not present any vesicles now, and he is unable to tell me if vesicles appear in his mouth. With poor illumination I saw what I thought were scars on the buccal mucosa and on the hard palate. Obliteration of mucous surfaces with scar formation is characteristic of pemphigus of the mucous membranes. This is most commonly seen in the nasopharynx, causing partial obliteration. I have seen atresia of the vagina resulting from the disease. Involving the conjunctiva the disease is characterized by a subconjunctival inflammation which is progressive, causing symblepharon, obliteration of the cul-de-sacs and adherence of the eyelids to the bulb. The conjunctiva over the cornea is transformed into a parchment-like membrane, with resulting blindness. This obliterating pathologic process involving all mucous surfaces and preceded by recurring vesicular eruption constitutes the concept of pemphigus of the mucous membranes of which conjunctival or ocular pemphigus is one phase. The disease may be confined to the mucous membranes, with or without conjunctival involvement or blebs on the skin.

I note the conjunctivas of both lower lids are reddened and thickened, and the bulbar conjunctiva of both eyes in the lower portion is redundant and can be wrinkled. This is characteristic of the early stage preceding symblepharon and obliteration of the cul-de-sacs. In a consistent way, he states, his eyes become inflamed, with symptoms of conjunctivitis. He also states that at times he notices blood in his handkerchief, which I believe is evidence of vesicular lesions on the nasal septum which rupture, leaving erosive areas which ooze blood.

I suggest examination of the mucous surfaces of the urethra and anus and observation to note the occurrence of vesicles in the mouth.

This disease represents a benign form of pemphigus. Vesicles in the mouth usually appear and disappear over many years. In one of my patients they appeared at intervals for eighteen years. This patient has been under my observation for nine years (*ARCH. DERMAT. & SYPH.* 27: 718 [April] 1933, 37: 364 [Feb.] 1938, 687 [April] 1938, 42: 228 [July] 1940). According to my observations, the disease pursues the same course in Jews.

DR. M. H. GOODMAN, Baltimore: I do not think the type of lesion which presents itself on the skin is sufficiently accounted for. I feel, with a little hesitancy, that Darier's disease of the mucous membranes should be ruled out, in view of the fact that the cutaneous lesions, with their peculiar small papular

appearance, crusting and history of coming and going for a period of ten years, should be taken into consideration. Darier's disease should, at least, be ruled out by histologic examination. The examination should be done, I think, by a dermatohistopathologist.

DR. EUGENE F. TRAUB, New York: There were four sections of skin removed for diagnosis, three from the mouth and one from the upper lip. I did not present them here because each showed simply an "inflammatory nodule." The interesting thing about this patient is that he has been under constant observation for about ten years, which is an unusual circumstance in New York. About seven years ago I told him that I thought he had pemphigus, and but little change has taken place since then. Especially since the lesions have been almost entirely confined to the mucous membranes, I am surprised that nothing further has happened. I trust that Dr. Klauder's interpretation is correct. If this case proves to be one of pemphigus, it is the most slowly progressive one, especially considering that the condition began on the mucous membranes, that I have been able to follow.

Naevus Pilosus. Presented by DR. GEORGE C. ANDREWS, New York.

R. O., an American girl aged 14, is presented from the Vanderbilt Clinic. At birth the patient had a pigmented hairy nevus involving the left malar region, extending beneath the left eye to the bridge of the nose and into the left eyebrow. At the age of 3 months treatment was started with solid carbon dioxide, first being applied to the nonhairy edges of the nevus. Exposures of fifteen to thirty seconds were given at two to four week intervals, the last treatment being in February 1931. At that time the color had practically cleared but the hairs remained. Epilation was started in November 1938. The patient has received fifty-two treatments by electrolysis.

Cavernous Hemangioma of the Left Inner Canthus. Presented by DR. GEORGE C. ANDREWS, New York.

M. R. K., a Russian girl aged 19 months, is presented from the Vanderbilt Clinic. The lesion was present at birth. When she was examined at the age of 3 months, there was a cavernous swelling on the left inner canthus, measuring 1.5 cm. in diameter. At the lower border there was a bright red elevation 5 mm. in diameter. Pressure of the mass resulted in narrowing of the inner part of the palpebral fissure. Thirteen injections of half strength quinine hydrochloride and ethyl carbamate (urethane) were given at two to four week intervals in doses of 3 to 5 minims (0.2 to 0.3 cc.). The last treatment was given five months ago.

Cavernous Hemangioma of the Eyelid. Presented by DR. GEORGE C. ANDREWS, New York.

R. F., an American girl aged $2\frac{1}{2}$ years, is presented from the Vanderbilt Clinic. The lesion was present at birth. When she was examined at the age of 2 months there was a red elevated mass on the left lower eyelid, measuring 6 by 18 mm.

The angioma was injected with half strength quinine hydrochloride and ethyl carbamate (urethane) at two to four week intervals. Ten injections were given, the last one eleven months ago.

The object of presenting these cases is to show that if one uses solid carbon dioxide and uses it lightly without producing ulceration, one can do so without producing a scar. I believe that radium used near the eye in infants and children is a dangerous procedure. Angiomas near the eyes should be treated by injection of sclerotics, plastic surgery or the application of solid carbon dioxide. I believe that the best cosmetic result is obtained by the injection of a sclerotic or by plastic surgery.

Blastomycosis Presented by DR GEORGE M LEWIS, New York

A A, an Italian aged 46, a baker, is presented from New York Hospital. He was born in Italy and came to the United States in 1907. The eruption was first noticed in 1922, while he was working for a railroad in West Virginia. The eruption began on the left side of the chest and spread gradually. The correct diagnosis of blastomycosis was made for the first time when he was in Italy in 1932. While he was there the eruption responded well to iodide therapy, but it recurred promptly on his return to this country in 1933. He has had roentgenotherapy, potassium iodide in large amounts, sodium iodide intravenously, arsenic, salves and sulfanilamide, without more than temporary improvement. There is always some improvement when some form of iodide therapy is given.

Examination shows lesions on the anterior part of the chest, left shoulder and axilla, entire back of the neck, right side of the chin, right upper lip, nose, periorbital regions, right temporofrontal region, right ear and right temporal and right occipital portions of the scalp. The lesions are of two types: (1) old burned-out areas where the skin is in places thin and atrophic and in other parts thickened and fibrotic, as in the left axilla and in the neck (resulting in limitation of movement), (there is some atrophy of the muscles of the neck due to disuse, and telangiectasia is present), (2) in the active disease, plaques of varying size, which are elevated and verrucous, moist on the surface and covered with greenish brown crusts. The largest lesion is on the back, almost centered, with smaller lesions on each side. The periorbital region is involved and besides the active verrucous crusted lesions in this location, as well as on the nose and other parts of the face, there is an ectropion of both upper and lower eyelids on the right side, exposing the conjunctival surfaces completely to the air. The patient is unable to close the lids, and there are reddening and swelling of the subconjunctival tissues and a constant overflow of tears. The scalp shows superficial, exudative lesions, covered with crusts.

Blastomyces dermatitidis was demonstrated in scrapings from lesions and in cultures. There was moderate leukocytosis. The test with blastomycin showed a positive reaction. The Wassermann reaction was negative, as were the results of other routine tests. Histologic examination showed the epidermis to be decidedly irregular, acanthotic and containing numerous small abscesses. The surface was covered with crusts. In places there were pseudoepitheliomatous changes. There was a good deal of granulation tissue, with many new blood vessels, plasma cells, small round cells and giant cells. *Blastomycetes* approximately the size of macrophages could be seen both in the epidermis and in the upper part of the cutis.

Recent treatment has consisted of (1) sulfapyridine (total dose of 65 Gm) from Jan 10 to Feb 2, 1940, which caused a flare-up of the condition, (2) intensive iodide therapy from February 5 to February 17, with improvement, (3) thymol from February 20 to date, increasing up to 4 Gm daily, with apparent improvement, and (4) aqueous gentian violet used locally with grease occasionally to soften the crusts.

DISCUSSION

DR J LAMAR CALLAWAY (by invitation), Durham, N C. In view of the fact that the intradermal blastomyces reaction is positive in this case, I suggest that the patient be desensitized with an autogenous vaccine prepared from his culture. It has been my experience with patients who have blastomycosis that they do not respond to iodides until they have been desensitized to their own organism.

DR J H SWARTZ, Boston. Has this patient had any pulmonary symptoms? Have any examinations of the chest been made?

DR GEORGE M LEWIS, New York. Roentgenograms of the chest were normal. Since the history was written I have attempted to demonstrate agglutinins and precipitins, but without success. In a further study of the autogenous vaccine,

I diluted it with the patient's own serum and found it made no difference in the cutaneous reactions which could be elicited. I am familiar with the work of D. S. Martin and D. T. Smith at Duke University, who reported a series of cases of blastomycosis (Blastomycosis: A Review of the Literature, *Am. Rev. Tuberc.* **39**: 275 [March] 1939; A Report of Thirteen New Cases, *ibid.* **39**: 488 [April] 1939). They found that after desensitizing the skin to blastomycin, the therapeutic response was better to iodide therapy. They also mentioned that it might be dangerous to give iodides to such patients without first desensitizing the skin to blastomycin. This patient was given iodides in doses as high as 600 grains (39 Gm.) a day and over long periods without any evidence of exacerbation of the lesions. While I was successful in curing an area by curettage followed by application of gentian violet, the surgeons refused to undertake extensive curettage under anesthesia. At the present time the patient has just completed two weeks' treatment with thymol, and it is of interest that he was able to tolerate a dose of 4 Gm. a day without symptoms. The usual dose is from 0.5 to 2 Gm. a day. There seems to be more improvement from thymol than from any other form of therapy which he has had.

Pachyonychia Congenita. Presented by DR. ANTHONY C. CIPOLLARO, New York.

J. P., an American boy aged 12 years, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. His mother says that the patient was born with deformed nails. The changes in the oral mucous membranes and the skin occurred soon after birth and have gradually increased in severity.

Examination shows on the inner surfaces of the lips and cheeks and on the dorsum of the edges of the tongue, dull whitish gray patches, irregular in shape and slightly elevated. In some places the patches have an irregular surface, somewhat suggestive of a verrucous condition. These leukokeratotic patches show no signs of malignant degeneration. The nails of both hands and both feet are abnormal. They are yellowish brown, distorted and hyperkeratotic. The nails are hard and oversized, as in cases of onychogryphosis. The skin shows the following changes: On the mesial surfaces of both great toes are areas in which there are sharply demarcated patches of denuded skin. These areas are glistening and show little tendency to heal and are gradually progressing peripherally. On the outer side of the right foot, just below the external malleolus, there is a similar patch measuring approximately 7 by 3 cm. The skin as a whole is dry. On the external surfaces of both arms, there are many fine keratotic lesions. Verrucae of varying sizes are present on the tips of the elbows and the extensors of the forearms.

The Wassermann and Kahn reactions were negative. Cultures from the tongue for fungi were negative.

Treatment has consisted of topical applications.

DISCUSSION

DR. A. BENSON CANNON, New York: I agree with the diagnosis in this case. I should like to call attention to the lesions of the mucous membranes that so closely resemble the condition that I described a few years ago as white sponge nevus of the mucous membranes of the oral cavity, vaginal mucous membranes and anus (Cannon, A. B.: White Sponge Nevus of the Mucosa [Naevus Spongiosus Albus Mucosae], *ARCH. DERMAT. & SYPH.* **31**: 365 [March] 1935). The only difference that I can note in this patient's lesions of the mouth from the condition in my patients is that they had sievelike, clear, hyaline, discrete, raised, pinhead-sized areas in the white spongy parts that resembled vesicles. Their disease was congenital and appeared in three different generations of the same family. Since publication of the history of those cases, I have studied two

other family groups with the same condition, no member of either group having any other defect

DR DONALD M PILLSBURY, Philadelphia I agree with the diagnosis as presented In connection with this case, I recall a report by Goldberg (Goldberg, S C Resistant Erosive Lesions in Pachyonychia Congenita of Jadassohn, Treatment with Buffered Cysteine Hydrochloride, *ARCH DERMAT & SYPH* 36 331 [Aug] 1937), in which ulcerated lesions in a case of this disease healed after applications of cystein hydrochloride to promote epithelization

DR GEORGE C ANDREWS, New York There are reasons to believe that this condition is a variant of Darier's disease, keratosis follicularis Papules develop on the extremities which are indistinguishable from the lesions of Darier's disease

Naevus Cerebriformis (Cerebelliformis) of the Scalp Presented by DR ELLWOOD C WEISE, Bridgeport, Conn

H F, a woman aged 24, a private patient, is presented with a large nevoid process involving the scalp since birth On the scalp, beginning about 9 cm back of the front hair line and extending transversely over the scalp from ear to ear and from thence backward, involving the entire vertex, occipital and suboccipital regions, is a large pinkish, irregularly convoluted mass, 25 by 25 cm, practically devoid of hair except from the depths of the sulci between the convolutions where a fair amount of hair arises to provide a partial covering for the tumor mass The convolutions are irregular and unusually large, as evidenced by the lowermost transverse convolution in the suboccipital region, which hangs down in an almost apron-like effect and measures 25 cm from side to side, its width being 4 cm and its depth over 5 cm The borders of the lesion arise almost precipitously from what appears to be normal skin of the scalp anteriorly and normal skin of the neck posteriorly and at the sides as well The patient's mentality is average or above There is a somewhat foul odor present There is no familial history of similar tumors The patient's daughter, however, presents a small naevus flammeus of the left forearm

The histologic report was as follows The sections of a cutaneous tumor showed atrophic epidermis A moderate hyperkeratosis was present Large sebaceous glands could be seen The stroma of the tumor showed marked fibrosis It contained numerous dilated thin-walled vessels In the upper portions of the stroma were numerous polygonal cells arranged in nests These were typical nevus cells Here and there could be seen pigment-containing cells A few chromatophores were noted Mast cells were scattered throughout the section The deeper portions of the growth showed connective tissue which contained numerous bundles of spindle-shaped cells Here the growth suggested the picture sometimes interpreted as a neuroma Most of the cells, however, appeared to be spindle-shaped nevus cells The histologic diagnosis was nevus pigmentosus (Dr Gerald F Machacek)

DISCUSSION

DR ELLWOOD C WEISE, Bridgeport, Conn This case was presented principally for two reasons One was because of the large size of the nevus and the other was for suggestions as to treatment The case was primarily that of a surgeon and was referred only recently to me for an opinion I have seen only a few cerebriform nevi which might approach the size of this one Aside from the size of the lesion and its appearance, there is an odor from it, and it is objectionable to the patient on this account She is only 24 years old and is anxious to have the lesion removed The question in the mind of the surgeon is whether to remove it in one stage, followed by skin grafting, or to do so in several stages, performing a partial excision of one quarter of the lesion at one time, drawing the edges together for suturing if the tissues permit and eventually removing the entire lesion in stages in this fashion It is surprising how little one can find in the dermatologic textbooks or literature on this subject

It is hardly mentioned. However, there is a splendid article dealing with this subject by Hammond and Ransom (*Arch. Surg.* **35**:309 [Aug.] 1937). I should like to know if any of the members here have had any experience removing a nevus of this type and of this size and whether it should be done in one or several stages.

DR. WILBERT SACHS, New York: I have just written an article for the ARCHIVES on this condition (Sachs, W., and Sachs, P. M.: Turban Tumors, *ARCH. DERMAT. & SYPH.* **42**:15 [July] 1940). All types of nevi, such as epidermal nevi, cutis or dermal nevi, may be found in the same specimen. One must be careful that there are no junction type nevi (melanoma or forerunner of nevocarcinoma) in the specimen. In 1 case such a nevus was found, and when the growth was removed, numerous metastatic lesions of nevocarcinoma developed and the patient died.

DR. JOSEPH V. KLAUDER, Philadelphia: The lesion in this patient is comparable in size and depth to the one involving the side of the face of a patient whose photograph is in my paper "The Treatment of Nevi with Particular Reference to High Frequency Current" (*J. A. M. A.* **90**:1763 [June 2] 1928). I believe the choice of treatment of this lesion is by electrodesiccation. I advise such treatment under general anesthesia in three stages. At the onset of destruction I should select bipolar electrodesiccation, changing to unipolar as one approaches the level of the skin. When the operative area of the first destruction is almost healed, I would then perform the second destruction. With this technic I doubt if skin grafts will be necessary. They were not for the patient aforementioned. Roentgenotherapy of the scarred area, if keloidal, will be necessary. I believe the only cosmetic defect will be the absence of hair, for which a wig could be worn.

DR. MAX SCHEER, New York: I recall a patient at the clinic several years ago who had an extensive nevus of this type on the back, much more extensive than this one. Part of the lesion was removed by electrodesiccation, and in the desiccated area a nevocarcinoma developed, which later metastasized to the glands.

DR. A. BENSON CANNON, New York: I can see no indication for removing the nevus that she has had all of her life and which has not handicapped her to any great extent. I do not believe that it is possible to remove the nevus surgically without destroying the greater part of the scalp, and probably this would leave a more disfiguring condition than is now evident.

CHICAGO AND DETROIT DERMATOLOGICAL SOCIETIES

HERBERT RATTNER, M.D., Chairman

Joint Meeting, Ann Arbor, Mich., March 17, 1940

Presentation of all cases at this meeting was made by Dr. Udo J. Wile, Ann Arbor, Mich., with the exception of those by Dr. H. L. Keim, Detroit, and Dr. Wile; Dr. A. E. Schiller, Detroit, and Dr. Wile; Dr. H. J. Parkhurst, Toledo, Ohio; Dr. Loren W. Shaffer, Detroit, and Dr. C. A. Doty, Detroit.

Primary Tuberculosis of the Skin.

R. D., a white man aged 44, first noticed a red, nonpainful, nonfluctuant papule beneath the left eye three months ago. There was no preceding injury. Four weeks later there developed at the angle of the left jaw a painless swelling, which rapidly increased in size. The patient has been a bartender for eleven months, and the man with whom he works is said to have a tuberculous lesion of the throat. The patient has done no hunting and has not come in contact with rabbits. There has been no exposure to syphilis, so far as he knows.

Examination on Feb 9, 1940 revealed a well developed and nourished man, who did not appear ill. On the cheek, 1 inch (2.5 cm) below the left eye, there was a pea-sized, indurated, nontender, erythematous papule, covered by a thin crust. Anterior to and below the left ear were two groups of glands, the capsules of which appeared to have fused, forming hard, nontender masses fixed to the underlying tissue. There was no fluctuation. The overlying skin was not attached. There were no draining sinuses.

Dark field examination of tissue from the lesion below the eye gave negative results. Serologic tests gave negative results on three occasions. A roentgenogram showed no signs of old or new tuberculosis. Direct examination of the bloody suspension obtained from a puncture of a gland showed no acid-fast bacilli. The tuberculin test showed strong reactions in twenty-four to forty-eight hours (with a dilution of 1:1,000,000). The result of an agglutination test for tularemia was negative. Direct examinations and cultures for sporotrichosis, actinomycosis and blastomycosis gave negative results. The blood count was normal except for evidence of mild anemia. Culture of material for tubercle bacilli and inoculation of guinea pigs have given negative results to date.

DISCUSSION

DR GEORGE H. BELOTE, Ann Arbor, Mich. The photograph was taken about three weeks ago, the lesion was considerably larger than it appears now. Also, the adenitis is prominent in the picture, the enlargement of the glands has decreased about 50 per cent. This case, I confess, was a surprise to me—more, I think, on account of the patient's age than for any other reason. I have had the belief that the so-called primary tuberculosis complex is likely to occur in children, usually in very young children. A study of the literature, however, showed a considerable number of cases in adults, so age does not rule out the disease in this case.

When this patient was admitted to the hospital, I thought that he had a primary syphilitic sore, but laboratory studies failed to substantiate that diagnosis. The only positive evidence is the patient's abnormal sensitivity to tuberculin. It is interesting that he shows no roentgenologic evidence of either new or old tuberculosis. The location of the lesion is the same as that in most recorded cases, either with preauricular or submaxillary adenitis. On diascopic examination of the primary lesion the diagnosis can be made, even though the lesion has now healed.

Lupus Vulgaris of the Cheek

M. L., a white woman aged 28, first noticed a small lesion on the left side of the face in 1938. By January 1939 this had increased to the size of a dime. From July to December 1939 the patient received nine treatments with roentgen rays, with little benefit. She has had pulmonary tuberculosis since 1938. Although the process has now been quiescent for the past nine months, she is still a patient at the Wm. H. Maybury Sanatorium, Northville, Mich.

The patient was first seen at the University Hospital on Jan. 16, 1940, when she presented a single lesion in the left malar region. This was circular and measured 2 cm in diameter. It was made up of numerous pinhead-sized, flat, dully erythematous papules on an erythematous, moderately infiltrated base. On diascopic examination these papules appeared light brown.

The urine showed a trace of albumin. A complete blood count was normal. Examination of the sputum showed no tubercle bacilli. The pleural fluid showed tubercle bacilli in July 1939. The Kahn reaction was negative. No tissue was available for histologic study.

Treatment with water-cooled ultraviolet radiation has been given with a quartz-mercury vapor lamp (a Burdick lamp, with an output of about 1 erythema unit per second), with 50 erythema units on Jan. 16, 1940 and 60 erythema units on February 28. There has been a good response to this treatment, the lesion now being reduced by more than one half.

Lupus Vulgaris of the Nose.

G. B., a Negro girl aged 12 years, has had a chronic sore on the nose since she was 7 years of age (1935). In 1936 she received twenty-five injections of gold sodium thiosulfate, together with sixty-nine treatments with air-cooled ultraviolet radiation, with some improvement. During 1938 and 1939 she received a total of twenty-five roentgen ray treatments, with little benefit. She was first seen in the University Hospital on Feb. 15, 1940.

The patient presents a destructive granulomatous lesion involving the nose, cheeks and upper lip. The distal portion of the nose has been destroyed, leaving an ulcerated, heavily crusted surface. The lesion extends out on each cheek, where definite nodules and papules are present. The left nostril is stenotic. The process extends into the right nostril about 1 cm. The larynx shows involvement, and the diagnosis of lupus of the larynx was made by members of the department of otology.

In 1937 she apparently had pulmonary involvement. Present roentgenograms show no sign of parenchymal lesions, though a fairly large, partially calcified tuberculous gland is present at the upper pole of the hilus of the left lung.

The urine was normal. The blood count showed 72 per cent hemoglobin and 4,300,000 erythrocytes and 4,900 leukocytes per cubic millimeter, with a differential count of 78 per cent neutrophils, 19 per cent lymphocytes and 3 per cent monocytes. The Kahn reaction of the blood was negative.

Treatment has been started with water-cooled ultraviolet radiation given through a quartz applicator with pressure (a Burdick lamp, with an output of about 1 erythema unit per second). On Feb. 19, 1940, 50 erythema units was given to all areas not encrusted; on February 29, 50 erythema units was given, and on March 7, 80 erythema units. There has been good response to this therapy.

Lupus Vulgaris.

A. E. W., a man aged 53, was first seen in 1934, at which time he said that eight years previously he began to notice the lesions on the lower lip. In spite of local medication, ultraviolet irradiation and twelve intravenous injections of a gold compound, the lesions spread to involve the nose, forehead, cheeks and neck, with destruction of tissue. He had been taking care of his wife, who had died of pulmonary tuberculosis eight years before. He was never aware of having pulmonary tuberculosis himself.

Physical examination revealed that the forehead, lips, cheeks, nose and mucous membranes of the mouth and nose were the sites of active lesions, while scars marked the sites of previous lesions on the neck. The active lesions were granulomatous, slightly elevated and covered with scales and crusts. The borders were well defined and serpiginous in places. Central atrophic scarring was present here and there. The lungs were clear.

Curettage and cautery resulted in the healing of some of the lesions. During the past year water-cooled ultraviolet radiation given with pressure has brought about considerable healing of the lesions.

Kahn reactions of the blood were negative. A stereoscopic roentgenogram in April 1939 revealed a calcified, localized and inactive lesion in the apex of the left lung. A roentgenogram of the spine taken in February 1940, on account of the patient's complaint of backache, showed moderate destruction of the intervertebral space between the fourth and the fifth lumbar body.

DISCUSSION ON CASES OF LUPUS VULGARIS

DR. RICHARD S. WEISS, St. Louis: I think the second case would be a good one in which to try injections of starch solution, as reported by Kile (Kile, R. L.: Treatment of Lupus Vulgaris by Injection of Starch U. S. P. [Corn Starch], ARCH. DERMAT. & SYPH. 39:471-473 [March] 1939. The condition is the type of lupus vulgaris that yields best to that treatment.

DR GEORGE H BELOTTE, Ann Arbor, Mich I should like to ask Dr Weiss whether starch solution has been used on the lesions of the mucous membrane

DR RICHARD S WEISS, St Louis No, I have not had the opportunity I think it should be tried

DR UDO J WILE, Ann Arbor, Mich I think a point worth mentioning in all 3 of these cases, one which is somewhat unusual in my experience, is that though they are all well defined cases of lupus vulgaris, in every one there is evidence of pulmonary tuberculosis, either in the roentgenogram or in the history Two of the patients have been in institutions for tuberculous patients Many years ago, in looking over the material in most of the sanatoriums where pulmonary tuberculosis was treated, I found that those in charge were almost wholly unfamiliar with the picture of lupus vulgaris Of late from one source I have noted a number of cases of lupus vulgaris associated with pulmonary tuberculosis As I recall, most of the patients I saw abroad, where lupus vulgaris is much more common than it is here, were relatively free from pulmonary lesions

DR FRANZ L BLUMENTHAL, Eloise, Mich These 3 cases are examples of the various types and stages of lupus vulgaris The condition in the first case is characteristic of the flat type There is an exogenous infection which occurred in about the same location as that in the case of primary tuberculosis of the skin The different clinical picture is due to the allergic state The case of the Negress is interesting from the therapeutic point of view

I have found that when the skin and mucous membranes are so extensively destroyed, there is not much hope of getting a definite result from local treatment A salt-free, high vitamin diet combined with general sun baths or ultraviolet irradiation give the best results For the ulcerated lesions of the mucous membranes and the skin roentgen ray treatment is indicated

In the last case the therapeutic result was good The patient is practically free of lesions except those on the mucous membrane of the mouth I suggest treatment with lactic acid, radium or roentgen rays The internal tuberculosis must be treated carefully

Noncaseating Tuberculosis of the Skin

In I B, a woman aged 55, a small area of superficial erythema was first noted on the right leg four or five years ago This gradually enlarged, and deep-seated nodules developed in and around it A similar lesion appeared on the left leg about a year ago At no time have the nodules broken down and suppurated Local applications and air-cooled ultraviolet irradiation caused no improvement Twelve intravenous injections of gold sodium thiosulfate caused the nodules to regress noticeably but had no effect on the rest of the eruption Twenty years ago the patient had pulmonary tuberculosis, which was treated with rest There has never been any cough or expectoration

Physical examination reveals an eruption confined to the lower extremities between the knees and the ankles This is chiefly on the anterolateral surfaces and is characterized by large superficial patches of dull erythema, with nodular lesions in and around the patches The nodules vary in size from that of an olive to that of a walnut and are not elevated There is no clinical evidence of active pulmonic disease

A Kahn reaction of the blood was negative A roentgenogram of the lungs showed no evidence of active pulmonic disease The leukocyte count was 14,000 per cubic millimeter

Sarcoid

E B, a woman aged 49, first had an eruption about seventeen years ago, at which time it involved her face, arms and buttocks Since then it has gradually become more severe The characteristic lesions have been small papules, discrete

at first and later confluent. Pruritus has been mild. At present the eruption is disseminated over the forehead, cheeks, nose and chin and is characterized by bluish red papules and plaques, studded with small nodules. Slight ulceration is seen on the nose. Similar papules and plaques appear on the arms and buttocks. There is no clinical evidence of pulmonary tuberculosis.

Treatment has included rest, high caloric diet, cod liver oil, gold sodium thiosulfate, water-cooled ultraviolet radiation, neoarsphenamine and cautery, with only moderate temporary improvement. She has had no active treatment for five years. The urine showed a trace of albumin, and study of the blood revealed mild anemia. The Kahn reaction of the blood was negative. The sedimentation rate was 0.77 mm. per minute. The tuberculin reaction was negative with a dilution of 1:100,000 and strongly positive with a dilution of 1:10,000. A roentgenogram disclosed no conclusive evidence of active pulmonary disease and no positive evidence of the involvement of the bones of the hands.

DISCUSSION ON THE CASE OF NONCASEATING TUBERCULOSIS OF THE SKIN AND CASE OF SARCOID

DR. M. H. EBERT, Chicago: The lesions in the case of sarcoid were almost identical with those in a young man with Besnier-Boeck-Schaumann sarcoid whom I presented two years ago at a meeting of the Chicago Dermatological Society (ARCH. DERMAT. & SYPH. 37:706 [April] 1938). In his case there were other evidences of systemic disease: enlargement of the spleen, general adenopathy and the peculiar mottling of the skin that one sees in cases of Besnier-Boeck-Schaumann disease. The lesions on the face in the case presented today bring to my mind the description of lupus pernio, but the discoloration is not marked enough for that disease. Lupus pernio of the Besnier type is a manifestation of sarcoid. The young man with the Besnier-Boeck-Schaumann sarcoid was treated with tuberculin, with considerable improvement in the cutaneous lesions and diminution in the size of the spleen. He improved and no one has been able to locate him; however, I do not think he has been cured. Conditions of this kind are usually resistant to any type of treatment.

The condition of the first patient, with the fairly well defined plaques on the legs, was certainly an "eye opener" to me. It did not suggest any form of tuberculosis until I looked at the microscopic sections, which settled the matter beyond doubt.

DR. UDO J. WILE, Ann Arbor, Mich.: Do you think that the disease in the second case should be labeled sarcoid?

DR. M. H. EBERT, Chicago: Yes.

DR. CLARK W. FINNERUD, Chicago: To me the most instructive case shown today was that of the woman with the lesions on the legs. It is likely that any one here would have been mistaken in the diagnosis were it not for the histologic section.

DR. FRANK STILES, Lansing, Mich.: I should like to present more information about the second case. I had the opportunity of seeing the patient two years ago. She had the lesions she presents now, and in addition she had an abscess in the pharynx which bulged out—a cold abscess. About six months later a generalized acute pustular eruption developed which I could not distinguish from variola. The lesions were grouped and arranged like those of variola.

DR. UDO J. WILE, Ann Arbor, Mich.: Was the patient febrile?

DR. FRANK STILES, Lansing, Mich.: The temperature was 102 F.

DR. UDO J. WILE, Ann Arbor Mich.: Was the eruption similar to that of smallpox?

DR. FRANK STILES, Lansing, Mich.: The condition took a little longer to develop than does the eruption of ordinary smallpox.

DR. M. H. EBERT, Chicago: Did she already have the lesions on the nose?

DR. FRANK STILES, Lansing, Mich.: No.

DR M H EBERT, Chicago Was an examination made for tubercle bacilli in the acute lesions?

DR FRANK STILES, Lansing, Mich No The lesions were multilocular, they were not necrotic The reason I mentioned this case is the absence of scarring Lesions of variola or tuberculids result in scarring

DR HERBERT RATTNER, Chicago The yellowish tinge and the shiny surface of the lesions in the first case bring to mind a case reported by Bruce-Jones (*Brit J Dermat* 49 238 [May] 1937) A woman with a tuberculous background had lesions which clinically resembled morphea However, the microscopic picture, unlike that in this case, was an indeterminate one suggestive of necrobiosis lipoidica Goldsmith has reported a similar case (*Proc Roy Soc Med* 28:363, 1934-1935)

DR GEORGE H BELOTE, Ann Arbor, Mich With reference to the case of noncaseating tuberculosis, I am surprised that some one has not suggested the possibility of necrobiosis lipoidica without diabetes While I thought there was no question of the diagnosis, there is, nevertheless, this morning a yellowish tinge to these lesions If I had seen the patient this morning for the first time, I would have been suspicious of necrobiosis I included a short reference to Goldsmith's case in the report of one I made a year ago (*ARCH DERMAT & SYPH* 40 887 [Dec] 1939) In this case the diagnosis was morphea-like tuberculosis of the legs As a result of microscopic study it was discovered that the condition belonged to the necrobiosis group

As to the other case reported here, microscopically there is no question of the diagnosis The condition is Boeck's sarcoid I admit, though, that the lesions are unusual, perhaps a little more widespread

A Case for Diagnosis (Lupus Miliaris Disseminatus Faciei? Lichen Planus?)

Mrs L D, aged 24, has an eruption which started about a year ago with a mildly pruritic scaling of the right upper eyelid This gradually progressed until both eyelids of both eyes were involved As the process went on, dark brown pigment became increasingly prominent Concomitant with the onset of the eruption the patient noted blurring of vision and spots before her eyes

Physical examination shows that the eruption is confined chiefly to the eyelids but involves also the remainder of the face to a less degree The smallest lesion is a pinhead-sized papule, suggestively flat topped, shiny and dark brown Some of the lesions, by coalescence and extension, have formed plaques from 0.5 to 1 cm in diameter Diascopy accentuates the color, although no distinct "apple jelly" nodules are noted

Ophthalmologic examination revealed iridocyclitis of the left eye, cyclitis of the right eye and keratic precipitates in the left eye, probably on a tuberculous basis

The results of tuberculin tests performed elsewhere were repeatedly negative A roentgenogram of the chest was normal The blood count showed 4,370,000 erythrocytes per cubic millimeter, 92 per cent hemoglobin and 5,750 leukocytes and with a differential count of 56 per cent neutrophils, 18 per cent large lymphocytes, with an occasional atypical cell, 18 per cent small lymphocytes, 6 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils The Kahn reaction of the blood was negative

DISCUSSION

DR M H EBERT, Chicago Some years ago Dr Nomland had a small series of cases of lesions on the face and around the eyes I think the lesions were single Histologically, there was a dense infiltrate of lymphocytes resembling leukemia cutis The lesions proved to be benign and never multiplied No new lesions appeared In an article on lymphocytoma (*Beitrag zur Pathogenese der Lymphocytome, Arch f Dermat u Syph* 173 181-195, 1935), Epstein described a nodular variety made up of a dense aggregate of lymphocytes In the slide I

saw there seemed to be a dense local infiltrate of lymphocytes. Perhaps the condition in this case is similar to the lymphocytoma described by Epstein.

DR. CLARK W. FINNERUD, Chicago: I had not thought of the diagnosis Dr. Ebert has suggested, but think it is a good one. From the appearance of the section there is more likelihood of the condition's being lupus erythematosus than either lupus disseminatus faciei or lichen planus. I am in favor of a diagnosis of lupus erythematosus, even clinically.

DR. GEORGE H. BELOTE, Lansing, Mich.: I confess that this case has been puzzling. I thought at first that the condition was tuberculosis. However, the microscopic picture has never substantiated that idea. The type of pigment is more compatible with that produced by lichen planus than anything else. The other suggestion of lupus erythematosus is probably a good one, and ought to be considered. I had not made that diagnosis. The other possibility, and one that is probably not borne out by the microscopic section, is lichen planus.

A Case for Diagnosis (Tuberculosis? Tertiary Syphilis? Both?).

About twenty years ago A. L., a white woman aged 54, noted a coin-sized, bright red spot on the anterolateral surface of the left tibia. The lesion gradually enlarged, lost its bright color and became indurated but never ulcerated. The lesion has never cleared, but has steadily progressed. It has never pained much, but the leg swells a great deal when she walks. The edema has always decreased promptly on elevation of the extremity.

There is no family history of tuberculosis, nor is there a history of contact with the disease. The patient's general health has been good.

Physical examination shows purplish discoloration of the skin of the left leg, associated with considerable induration, extending from the achilles tendon to a short distance above the popliteal space. There is induration of the entire leg, and in the vicinity of the popliteal space discrete nodules may be felt. There is no pain, no tenderness and no evidence of ulceration.

The Kahn reaction of the blood was 4 plus.

DISCUSSION

DR. ARTHUR R. WOODBURN, Grand Rapids, Mich.: The fact that the patient has not had antisyphilitic treatment makes me feel that the condition is syphilis. The area gave me the impression of a deep serpiginous, nodular syphilitic lesion. There is a nodular group of lesions deep in the subcutis which involves the muscle and tendon. The microscopic appearance is compatible with that of the diagnosis, and I think antisyphilitic treatment should be tried.

DR. HARRY FOERSTER, Milwaukee: Both syphilis of a late infiltrating type and tuberculosis of the erythema induratum type must be considered. The unilateral distribution and diffuse character of the lesions favor a diagnosis of syphilis, as do the perivascular round cell and plasma cell infiltrates, the absence of caseation necrosis and the few giant cells. The depth of the inflammatory infiltrate favors erythema induratum. The therapeutic test for syphilis may be necessary to determine the diagnosis.

DR. M. J. REUTER, Milwaukee: I agree with Dr. Foerster that the lesions are probably a late manifestation of syphilis. Because of the depressed areas and the boardlike infiltration, I thought of nodular panniculitis or Weber-Christian disease in the differential diagnosis. If these lesions occurred on the trunk or thighs this diagnosis would be likely.

DR. UDO J. WILE, Ann Arbor, Mich.: I have not seen this patient before, but I did study the histologic section. It seemed to me that there is more evidence in favor of syphilis than of tuberculosis. I believe this condition is a deep ulcerative syphilid, and because there is a good deal of softening, I think she would get well promptly if given antisyphilitic treatment.

The features that Dr Foerster mentioned in connection with the histologic section were puzzling to me also. Erythema induratum is apt to infiltrate around the subcutaneous fat, but I have not seen that condition often associated with gumma.

A Case for Diagnosis (Lupus Erythematosus?) Presented by DR LOREN W SHAFFER, Detroit

C W M, a man aged 56, has an eruption involving the arms, neck and face which began in 1929 and has been present almost continuously since. It has fluctuated in severity and has been better in summer. He was completely free from the eruption from April 1936 to August 1937, after the removal of his tonsils.

Now, new lesions appear suddenly as erythematous papular or nodular infiltrations that tend to assume crescentic configuration. A central dry crust develops on the larger lesions. No bullous lesions have been seen. Moderate itching and burning are present. Smaller lesions may disappear completely in a few days, but larger lesions require from two to three months to undergo involution, and leave moderate pigmentation but no atrophy. Occasionally lesions appear on the chest and back. Small but atypical lesions have appeared on the legs in the last six weeks. Multiple furuncles have developed during the past year and have been active in the last two months. There has been a definite tendency toward the localization of active lesions to the extensor surfaces of the arms, the posterior portion of the neck and around the eyes. Crusted lesions have been limited largely to the arms.

In 1931 a histologic study performed at Ann Arbor, Mich., was reported as suggestive of lupus erythematosus. A Wassermann reaction of the blood was negative. The differential blood count was within normal limits. A roentgenogram of the chest was normal.

The patient was treated for nearly three years at the University Hospital with gold sodium thiosulfate, without response. The condition cleared completely after the administration of a small amount of a bismuth compound, roentgen ray therapy and tonsillectomy. Then there were recurrences during the winters of 1937-1938 and 1938-1939. The present severe activity has been getting progressively worse since November 1939. Sulfanilamide, quinine bisulfide, mapharsen, Abdol capsules containing vitamins A, B, G (B₂) and D, liver extract, ultraviolet radiation, staphylococcus toxoid and autogenous (boils) vaccines have been tried, without encouraging results.

DISCUSSION

DR CLARK W FINNERUD, Chicago. The lesions were soft and grossly appeared like sarcoid. The diagnosis of lupus erythematosus must have been based partly on the section that was presented. On being questioned, the patient stated that he thought the specimen was taken from a new lesion, though he could not be sure, since the section was made several years ago. A new lesion of sarcoid could present the same microscopic picture as that seen in this case, the histologic characteristics of the disease not having had sufficient time to become manifest. I suggest taking a biopsy specimen from an old lesion. My diagnosis would be sarcoid rather than lupus erythematosus.

DR HARRY FOERSTER, Milwaukee. The patient's statement, corroborated by Dr Shaffer's observation, that a characteristic of the eruption has been the sudden appearance and short duration of an evanescent type of lesion is against a diagnosis of sarcoid or lupus erythematosus. I believe that this condition may be an eruption of the granuloma annulare type.

DR M H EBERT, Chicago. Dr Finnerud will recall a patient Dr Ormsby had under observation for twenty years. A young woman had lesions of this type starting on the inside of the thigh, spreading to the buttocks and arms and at times becoming generalized. Earlier these lesions were active. The history was

identical with that in the present case. The lesions appeared suddenly, were crescentic and bluish red and resembled those of sarcoid. Early in the course the edema was so great that there was some maceration of the shallow ulcers, though she has only a few scars. Then they disappeared spontaneously and slowly. That case Dr. Ormsby has always classified as one of an unusual form of toxic erythema multiforme.

DR. UDO J. WILE, Ann Arbor, Mich.: When I saw this patient two years ago in the hospital he presented a different picture. At that time he showed lesions characteristic of erythematous lupus. However, he did not respond to gold therapy but improved with the taking of a bismuth compound. The lesions have changed so that I did not recognize him when I saw him today. The lesions on the arms and legs are strikingly similar to those of an old nodular syphilid. Other lesions are so infiltrated and arcual that one might think of their being lesions of mycosis fungoides. It would seem to me difficult to diagnose this condition as diffuse erythematous lupus at this time.

DR. LOREN W. SHAFFER, Detroit: I am grateful for the discussion of this case. It brings out the many diagnoses that I have considered. I think that another biopsy should be performed, particularly of tissue from one of the more chronic, deep lesions.

The possibility of syphilis is suggested by the persistent, deeply infiltrative, arciform character of many of the lesions. However, the serologic reactions have been repeatedly negative. The patient seemingly responds to bismuth therapy. He was given arsphenamine treatment, without any response.

The question of sarcoid has been considered, but the present nature of many of these lesions seemingly is against such a diagnosis. The lesions around his eyes were edematous ten days ago but have almost completely disappeared within the last ten days. The lesions about the face have been less persistent than those on the arms, which tend to run a course of two or three months.

The fact that this patient was well for a period after the tonsillectomy would favor the possibility of some focal infection's being an etiologic agent in the case. There is no other evidence of a focus of infection except an atypical history of infection of the gallbladder.

DR. OTTO H. FOERSTER, Milwaukee: The patient told me that the eruption disappears completely early in the summer, when he strips naked and exposes himself to the sun, but that in August the lesions begin to reappear. Photosensitization seems to be concerned in its production. An investigation of the hepatic function is suggested, for in some instances there is an association of dermatologic conditions with disease of the gallbladder and the bile ducts.

Pemphigus Erythematodes (Senear-Usher Syndrome).

About March 1939, A. K., a Jewish woman aged 31, first noted "red spots" on the chest. These remained limited to the chest for several months, after which the lower part of the back became involved. About thirteen months after the onset, lesions appeared on the face. Vesicles first appeared fifteen months after the initial lesions and were first noted on the arms. The patient has never had any lesions in the mouth or on other mucous membranes.

Physical examination reveals a healthy-looking woman with a generalized eruption, which manifests a distinct predilection for the scalp, nose, cheeks, chest and back. Most of the lesions are slightly eroded, nummular erythematous macules, with a superimposed greasy, yellowish crust. These are confluent on the cheeks and relatively discrete on the trunk. Some of them, particularly those on the forehead and chest, suggest recently ruptured bullae. Nikolsky's sign is readily demonstrable. There are no mucosal lesions.

There were slight anemia, a normal differential blood count and normal urine. The result of a Pels-Macht test was 66 per cent. The Kahn reaction of the blood was negative.

The patient received twenty roentgen ray treatments before coming to the University Hospital. During her stay here she was treated with baths, compresses, bland ointments and enteral and parenteral preparations of various substances: arsenic, mercury, moccasin venom, sulfanilamide, colloidal gold, foreign protein, sulfapyridine, vitamins A and D in large dosage and two courses of germanin. She was also given three blood transfusions, which appeared to have a beneficial effect. The Nikolsky sign has been easily elicited on some occasions and has been absent on others. Bullae have appeared from time to time throughout her stay in the hospital.

M S, a woman aged 32, first noted a vesicular eruption about the neck five years ago, which spread rapidly to involve the whole body. Since, her skin has never been completely healed. When first seen here three years ago she had a universal exfoliative dermatitis, which has been followed by remissions and exacerbations at irregular intervals. The Nikolsky sign has been elicited frequently. Vesicles, papules, pustules and verrucous lesions of a seborrheic type have been noted at various times. The mucous membranes have been involved. Severe pruritus has been present.

The patient was last seen seven months ago, at which time she had only mild subsiding erythema and keratoses about the neck and under the breasts. A few new vesicles were continuing to appear on the legs.

Treatment has included the usual bland regimen of baths, wet dressings and mild ointments. Moccasin venom, arsenic, mercury, thiamine hydrochloride and germanin were given orally and parenterally, without remarkable response. Ultra-violet irradiation was of no benefit. Superficial roentgen ray therapy caused temporary improvement.

Blood counts were essentially normal except for mild anemia and eosinophilia, which are now minimal. The Pels-Macht index was 59 per cent. The Kahn reaction of the blood was negative. A histologic section is presented.

NOTE—A report of this case was included in the article by Wile and Arnold (The Senear-Usher Syndrome, *ARCH DERMAT & SYPH* 40 687-703 [Nov] 1939).

DISCUSSION ON CASES OF PEMPHIGUS ERYTHEMATODES (SENEAR-USHER SYNDROME)

DR F E SENEAR, Chicago. This condition has been discussed so often and reported so thoroughly by Dr Arnold that there is not much to be added. I saw the first patient on a previous occasion. I thought she had a benign type of pemphigus. I was interested in the second patient. In spite of the fact that she shows little eruption, she has a few crusted seborrheic lesions of a keratotic type on the back. These appeared after the involution of the vesicular lesions, and they are characteristic.

In respect to the possibility that any of the cases in this group are really examples of lupus erythematosus, the point made by Dr Harry Foerster that evanescence is a strong point against a diagnosis of lupus erythematosus occurred to me. It is a characteristic of many of these cases that the lesions may have a rapid onset and an equally rapid disappearance.

DR RICHARD S WEISS, St Louis. There has been considerable discussion whether the Senear-Usher syndrome is pemphigus or lupus erythematosus. A few years ago a woman came to the Barnes Hospital suffering from typical pemphigus of the vegetative type and with lesions in the mouth, axilla, around the umbilicus (where there was a patent urachus), in the genitalia and in the genitocrural region. A diagnosis of pemphigus vegetans was made. She was not satisfied and went around the country seeking a different diagnosis. She discovered the bad prognosis of the disease and was examined by twenty or more dermatologists in various parts of the country east of the Mississippi, two of whom made a diagnosis of a disease other than pemphigus. She was treated with iron cacodylate, without results. She was then given large doses of vitamin D, became perfectly well and remained so for about four years, without a single lesion. She went to Florida

on a vacation, acquired a severe sunburn and came back to St. Louis with typical lesions of the Senear-Usher syndrome. Dr. M. R. Caro, whom she consulted because he had reported on the sulfanilamide treatment for pemphigus, saw her and made the same diagnosis. She came back to St. Louis and started treatment with Pollitzer's solution (2 per cent sodium arsenate and 2 per cent phenol in distilled water), with no results. She now has typical dermatitis exfoliativa. Her illness started with pemphigus of the vegetans type, a diagnosis which was verified by about fifteen competent physicians. Then the Senear-Usher syndrome developed, followed by generalized dermatitis exfoliativa. I think her history shows a definite relation between the Senear-Usher syndrome and pemphigus.

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: Some one mentioned a few minutes ago the evanescent character of these lesions; I wish I could agree. The woman I presented has been in the ward for months. The other woman has had all kinds of treatment. The first patient has been treated with germanin and her lesions have cleared on two occasions. However, the drug produced such a severe renal irritation that I have not been able to go on with its administration.

DR. F. E. SENEAR, Chicago: When I referred to evanescence I did not mean to imply that the lesions in all these cases are characterized by sudden appearance and rapid disappearance. The point I wanted to bring out is that the rapid appearance and at the same time the rapid disappearance constitute a striking characteristic. The patient on whose case Dr. Usher and I based our original report has been in Chicago ever since, and we have had her under observation many times. Dr. Stillians now has her in his care. We would see her on one day with only a few lesions on the body, and a day or two later she would come in with one cheek completely denuded.

Pemphigus Vulgaris.

Six months ago A. S., a man aged 63, first had an eruption which appeared as an eczematoid patch on the right temple. The lesions remained stationary until three months ago, when vesicles began to appear, first on the chest and later over the whole body, sparing the mucous membranes.

Treatment included baths, wet dressings, bland ointments, oral medication (prior to admission to the University Hospital), 1.2 Gm. of adrenal concentrate daily by mouth and intravenous injection of 1,000 cc. of a saline solution daily. Since administration of the adrenal concentrate and the saline solution was instituted fewer vesicles have appeared.

Physical examination shows generalized involvement with vesicles, bullae and many superficially denuded areas, some of which are now secondarily infected. The vesicles and bullae are flaccid, and many are without erythema at the base. The Nikolsky sign can be elicited. The mucous membranes are clear.

The Kahn reaction of the blood was negative. Urinalysis showed no bromides, iodides or arsenic. Total serum proteins were 7.2 mg. per hundred cubic centimeters; albumin amounted to 2.9 mg. and globulin to 4.3 mg. per hundred cubic centimeters, with an albumin-globulin ratio of 0.7. Serum calcium was 11.6 mg. per hundred cubic centimeters.

DISCUSSION

DR. RICHARD S. WEISS, St. Louis: I think that there cannot be any question about this patient having pemphigus. It is difficult to say what is and what is not pemphigus. The opinion seems to be common that if the patient gets well the disease was not pemphigus. I have had a number of patients with what was called pemphigus who have recovered and have stayed well. The experience in other cities seems to be more unfortunate, and a number of physicians have made the statement that none of their patients with a condition diagnosed as pemphigus ever got well. It is perhaps a good approximation to say that about 30 per cent of the patients with pemphigus treated in St. Louis apparently recover while under treatment. I admit that with the iron cacodylate treatment a high caloric, high vitamin diet and rest are also given. Some of the patients that have recovered

have been seen at various meetings by many of the physicians present, and the diagnosis of pemphigus was confirmed by the great majority. I believe that some of the patients do get well, perhaps as a result of the iron cacodylate treatment. This patient, it seems to me, deserves intensive treatment with iron cacodylate and has a chance to recover.

DR E. A. OLIVER, Chicago. One point to which attention should be called is that a patch developed in the right temporal region in this case three months before the onset of pemphigus. I was interested in this feature because I have seen the condition develop this way in several cases. An elderly Jewish woman, whom Dr. Senear saw with me, had a patch of moist, eczematoid dermatitis on the vertex of her scalp that had a foul odor and resisted all treatment for several months. One day she failed to appear at the office, and I was called to her home; she was literally covered with bullae—typical pemphigus. The disease ran a rapidly fatal course and she died in several weeks.

I am sorry I cannot agree with Dr. Weiss. The physicians in Chicago have not succeeded in curing any of the patients with pemphigus. The Davis treatment, blood transfusions, arsenic and sulfanilamide have been used without success. The disease in St. Louis must be different from that in Chicago, because in Chicago pemphigus is looked on as a fatal disease.

DR CLARK W. FINNERUD, Chicago. I should like to ask Dr. Weiss if he followed any of those patients over a period of years. I have encountered cases in which the pemphigus cleared temporarily, but soon recurred, followed by death. I remember some of the cases which were reported years ago at a meeting in St. Louis, some of them in children. In my opinion, the cases in which the condition was "cured" were instances not of pemphigus but of bullous impetigo, toxic bullous dermatitis and other bullous eruptions. One should not hesitate to admit mistakes in diagnosis. Everybody makes them. Although not meaning to be in any way disrespectful, I have come to designate any case of supposed pemphigus in which the patient gets well and stays well as one of "St. Louis pemphigus."

DR M. R. CARO, Chicago. I wish to report that the 2 patients who were the subjects of my preliminary report on sulfanilamide (Pemphigus. Treatment with Sulfanilamide (*ARCH. DERMAT. & SYPH.* 37:196 [Feb.] 1938)) are both dead.

DR OTTO H. FOERSTER, Milwaukee. I wish to refer more particularly to the cases of benign pemphigus in which isolated and relatively few, though characteristic, bullous lesions develop suddenly on apparently sound skin. In such patients new lesions may develop over several weeks or months, and then there may be no lesions for a long period, sometimes for as long as ten to twenty years. I have observed several cases of this kind. Recently I saw a patient who had not had lesions for about twenty years and then had a recurrence of lesions of this type, which again disappeared. The diagnosis of pemphigus in that case was made originally by Dr. Pusey. The mild condition is in striking contrast to the acute type, often initiated with oral lesions, of which more are seen today than formerly. It seems to me there is a changing geographic distribution of cases of pemphigus and also that the benign type is now observed less often. I should be interested to hear what Dr. Blumenthal has to say on this subject.

DR FRANZ L. BLUMENTHAL, Eloise, Mich. Dr. Foerster mentioned the importance of the geographic distribution. This conforms to my experience. Before the World War, one saw pemphigus practically only in Jewish people from Russia. After the war there were a few cases in the German population, Jewish and non-Jewish. With regard to benign pemphigus, I have seen patients whose lesions have remained localized for many years. I remember a patient who had lesions on the penis for ten to fifteen years before the eruption became generalized. Oral lesions are not so seldom localized for a long time. When the eruption becomes generalized there is not much hope. On the other hand, there are a few conditions which start clinically like pemphigus, but later the diagnosis is not maintained because of recovery.

DR. LOREN W. SHAFFER, Detroit: Two months ago I presented before the Detroit Dermatological Society a patient with a condition which was accepted as typical Senear-Usher syndrome. Since then pemphigus foliaceus has developed. She failed to respond to sulfanilamide. She is improving; whether the improvement is due to intensive treatment with vitamins (A and D) will be interesting to observe. I should like to ask whether any one has had any experience with riboflavin.

DR. OTTO H. FOERSTER, Milwaukee: I have had 2 patients with pemphigus who failed to respond to riboflavin.

DR. THEODORE CORNBLEET, Chicago: I have had a patient under observation with typical pemphigus that began in the mouth and seemed to be fulminating. The patient for the present seems to be responding to sulfapyridine. I do not know how long that improvement will be maintained; I have my doubts whether it will continue. My use of sulfapyridine in cases of pemphigus was suggested by a report of its usefulness in treatment of dermatitis herpetiformis. I have seen some improvement in 2 patients with this disease. If dermatitis herpetiformis continues to respond as well to sulfapyridine, as it seems to at present, the drug may be a therapeutic agent for the differential diagnosis of dermatitis herpetiformis and pemphigus.

DR. UDO J. WILE, Ann Arbor, Mich.: I have never observed a case that I thought was certainly one of pemphigus in which the termination was not unfavorable. I have tried everything that I know of and that is suggested in the literature: the Davis treatment, sulfanilamide and riboflavin; none of my patients with pemphigus have recovered. Perhaps there is some difference in geographic distribution. Also, it is possible that there is a difference in criteria. There are a number of conditions I should like to call pemphigus that I do not feel are pemphigus. They are pemphigus-like eruptions. I do not believe that all of Dr. Brocq's cases are those of pemphigus.

DR. H. RATTNER, Chicago: At the Cook County Hospital I treated 2 patients with pemphigus by means of smallpox vaccine, with good "takes" in both instances but with no beneficial results. I also treated 4 patients with rabies vaccine, without benefit. My experience is similar to that of Dr. Wile.

Universal Exfoliative Dermatitis, Probable Lymphoblastoma. Presented by DR. C. A. DORTY, Detroit.

Three years ago in M. M., a man aged 61, a red pruritic, scaling eruption developed over the thighs and hips. This has extended gradually and for the past year has been universal. In spite of loss of weight, the patient's general health has been fairly good.

He also gives a history of having had a penile sore about thirty years ago, which soon disappeared after local treatment and six intramuscular injections. No further antisyphilitic therapy was ever given. He had symptoms of hypertension, for which he was given a "pink liquid medicine" shortly before the onset of the dermatitis, but since then its administration has been discontinued. He has not worked at his trade as a carpenter since the onset of the eruption and has been confined to bed most of the time during the past six months.

Examination reveals a universal, scaly erythroderma, with fissures of the palms and soles and onychogryposis. The edge of the liver is palpable. There is also generalized lymphadenopathy.

The Kahn reaction of the blood was negative. A blood count showed 14.2 Gm. of hemoglobin per hundred cubic centimeters (91 per cent), 4,900,000 erythrocytes and 16,800 leukocytes per cubic millimeter, with a differential count of 72 per cent neutrophils, 11 per cent large lymphocytes, 9.5 per cent small lymphocytes, 5.5 per cent monocytes, 2.5 per cent eosinophils and 0.5 per cent basophils. The report from the Simpson Memorial Institute was: "The blood picture is not definitely suggestive of lymphoblastoma." The blood culture revealed no

growth While in the hospital the patient received topical applications, ultraviolet radiation and superficial roentgen ray therapy, with some benefit

DISCUSSION

DR. H. L. KEIM, Detroit I think that in this case the term dermatitis exfoliativa could be dropped and that the case could be classified as one of lymphoblastoma, of the universal leukemia cutis type It seems to me that the only requirement lacking for such a diagnosis is the number of circulating lymphocytes, and it is my belief that if the patient lives long enough these neoplastic cells will get into the circulation and definitely establish a diagnosis of universal leukemia cutis The histologic picture fulfils the requirements

DR. E. A. OLIVER, Chicago In a case of lymphogranulomatosis (Urbach, E. Lymphogranulomatosis [Hodgkin's Disease] Treatment with Sulfanilamide, *ARCH DERMAT & SYPH* 41 181 [Jan] 1940), the condition improved remarkably on treatment with sulfanilamide Urbach stated that he had used this drug because the English school believes that Hodgkin's disease is a virus disease

Early Mycosis Fungoides Presented by DR. UDO J. WILE, Ann Arbor, Mich., and DR. H. L. KEIM, Detroit

M. S., a white man aged 39, was first seen on Dec. 4, 1939, when he presented a generalized eruption on the trunk, arms and legs which resembled pityriasis rosea He was seen again on Feb. 12, 1940, at which time the eruption had changed considerably The lesions had now become brownish, infiltrated plaques and were scattered over the trunk, face, arms and legs Since that time he has received superficial roentgen ray therapy, with considerable improvement

DISCUSSION

DR. H. L. KEIM, Detroit The diagnosis of early mycosis fungoides was made on clinical grounds only when I first observed the patient, in the middle of January He had been seen by Dr. Wile before, when he presented what was thought to be a somewhat atypical and extensive pityriasis rosea, but in January the itching was severe and the lesions became heavily infiltrated There was also enlargement of all the superficial lymph glands Unfortunately, the histologic section shows little and is scarcely more than suggestive As so characteristically occurs in cases of mycosis fungoides, these lesions have responded, to their present status, to small amounts of superficial roentgen ray therapy Within the past two weeks there have developed, in spite of the treatment, numerous pea-sized nodules on the outer surface of each thigh and on the abdomen, which I feel should be removed for microscopic study in the belief that they will show more characteristic microscopic evidence of mycosis fungoides than the section presented today

DR. CLARK W. FINNERUD, Chicago Early lesions of mycosis fungoides can usually be diagnosed histologically with certainty I suggest that sections be prepared from the plaques on the thigh, they are likely to substantiate or rule out this diagnosis

DR. UDO J. WILE, Ann Arbor, Mich. In my experience I have never seen anything like this condition The patient came to me because he had a lesion in the mouth I thought he had periadenitis mucosa In passing he said "I wish you would look at the rash on my body" Dr. Belote and I agreed that it was pityriasis rosea Within six weeks these lesions had grown so that no one would question the diagnosis of the infiltrative stage of mycosis fungoides The fact that they have responded so well to roentgen therapy and left the pigmentation makes the diagnosis more likely I believe that this man has mycosis fungoides, in spite of the fact that the histologic section is not conclusive I am surprised that some one did not make the diagnosis of a fixed eruption, because the pigmentation did suggest that associated with phenolphthalein There was no suggestion of a

fixed eruption when we saw him originally. He had an enlarged spleen then, and he still has enlarged lymph glands.

DR. FRANCIS E. SENEAR, Chicago: I agree that the histologic picture does not support the diagnosis of mycosis fungoides. The eruption has undergone involution so much at present that it is difficult to have a definite opinion. One point might be brought out; that is, though recession has taken place in a number of the lesions, one can make out a definite tendency toward the development of crescentic and annular configurations, such as are seen in mycosis fungoides.

Necrobiosis Without Diabetes.

E. K., a white woman aged 33, states that an eruption appeared on the left leg about five years ago. At that time she thought it was a bruise, although she does not remember traumatizing the region. The same type of lesion appeared on the right leg two or three years ago. Her general health has been good. Her mother has diabetes mellitus, which is controlled by insulin.

Physical examination reveals two cutaneous lesions. That in the midline of the upper third of the right leg is now represented by a scar; the lesion was excised for histologic study. Over the middle of the anterior aspect of the left shin is an irregular plaque, about 4 by 2 cm., which is distinctly yellowish red. This appears to be inlaid, and on the surface numerous small vessels can be seen. There is also some associated scaling. Clinically the lesion is typical of necrobiosis without diabetes, and the patient assures me that the lesion on the right was similar. The liver is just palpable.

Urinalysis showed no sugar. Dextrose tolerance was normal. The fat content of the blood was as follows: 728 mg. of total fat, 183 mg. of total cholesterol and 44.1 mg. of free cholesterol per hundred cubic centimeters. Hepatic function, with the bromsulphalein test, was within normal limits.

DISCUSSION

DR. M. R. CARO, Chicago: I think that clinically the lesion is necrobiosis lipoidica diabetorum. Histologically, however, the changes are not characteristic. The lesion is much more inflammatory than one ordinarily sees in necrobiosis. There is, however, a microabscess on one side of the lesion, which suggests that there might have been a coincident infection when the biopsy specimen was removed. If these inflammatory changes are disregarded, the appearance of the slide is compatible with the diagnosis of necrobiosis. If any more tissue is available it would be well to make a sudan III stain; if not, biopsy should be repeated.

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: As a matter of fact, the biopsy was not performed here; only the slide was sent, with no tissue for study or for fat stain. From my previous experience I suspect that there might be difficulty in demonstrating fat. It seems increasingly obvious that the pancreas has more than one function. Every one who has followed the studies in recent publications will probably come to the conclusion that when one says insulin diabetes, one has said the last word. This is the one type of fat infiltration which is being treated with lipocaic. It is only two weeks since treatment was begun, so the time is too short for prediction of the result.

DR. THEODORE CORNBLEET, Chicago: I believe that this particular case is one of necrobiosis based on abnormal fat metabolism rather than on defective sugar metabolism. It is interesting to note that in this case some lipid values are, if anything, below normal or near the lower limit of normal. In some cases in which the values for blood lipoids are high, lipocaic lowers them. Dragstedt has shown that lipocaic may have favorable action, even though one of the lipoids, cholesterol, is not increased. Nevertheless, one of the principal actions of lipocaic is to reduce high lipid levels in the blood. In psoriasis that was the point of attack, for other physicians had also found that blood lipid values were raised

in this disease. Whether the reported favorable action of lipocaine on psoriasis is accomplished by the mere reduction of blood lipid values remains to be seen. Similarly, it is possible that the lipid pattern may be altered qualitatively, if not quantitatively, for favorable action in necrobiosis.

Leukoderma Acquisitum Centrifugum

V. S., a woman aged 33, had a mole excised from her back five years ago. The site of excision took considerable time in healing. Subsequent to the removal of the mole the patient noticed that a zone of depigmentation developed around each of several moles situated on the back and on the abdomen. This zone of depigmentation increased in size for several months and then all activity ceased. The lesions are asymptomatic.

Physical examination reveals several lesions, primarily on the trunk, each characterized by a central soft, pigmented nevus surrounded by a zone of depigmentation, which varies in size from 2 to 8 cm.

The basal metabolic rate was —10 per cent. The urine was normal.

Multiple Pigmented Nevi

W. A., a white woman aged 32 is presented, the report of whose case has already been published (Arnold, H. L. Multiple Pigmented Nevi, *ARCH. DERMAT. & SYPH.* 40:386 [Sept.] 1939).

DISCUSSION

DR. M. H. EBERT, Chicago: I think there is no question in this case that the condition is an interepidermal multiplication of "*cellules claires*." In the ordinary pigmented nevus these new-formed cells proliferate into the corium, a process which Unna designated as *Abtropfung*. Why this did not occur in the case under consideration is impossible to state, I have no idea what causes proliferation of these cells.

DR. M. R. CARO, Chicago: About five years ago I saw a patient with generalized nevi similar to those in this case. After an injury to a lesion on the right shoulder a rapidly growing tumor appeared, which was resected widely by electrocautery. There was no recurrence. A few weeks ago, soon after she injured one of the preexisting nevi on the right leg, this nevus also developed into a rapidly growing tumor, which was excised and proved to be a malignant melanoma.

Vitamin B Deficiency

M. B., a white woman aged 68, has been troubled with abdominal pain and discomfort after eating for many years. There have been episodes of diarrhea recently. Although adequate food has been available, her appetite has been poor and her diet inadequate in meat, eggs, milk and vegetables. Her skin has been dry, and on several occasions in the last ten years she has had attacks of sore tongue and burning of the esophagus and stomach.

Examination shows the patient to be undernourished, with dry, pale skin. The tongue is bluish red, with atrophy of the filiform papillae and relative smoothness of the surface. There is mild maceration of the angles of the mouth, with some erythema. Inspection of the legs discloses fine ichthyosiform scales.

Vitamin (A and B) Deficiency

F. G., an Italian woman aged 30, was first seen in 1934 with an intermittent vesicular eruption on the hands, which occurred each winter and was of eight years' duration. The diagnosis of tinea was made, and the skin responded readily to the usual treatment. There was no family history of a similar trouble.

She was next seen in 1939 and at that time had an eczematoid dermatitis on the hands. This was not considered to be of fungous origin, although the

exact cause was indeterminate. She returned in February 1940, having had the same sort of trouble for four months.

The history revealed a diet limited in fruit, meat, eggs, milk and fresh vegetables, with the addition of fruits and vegetables only during the summer months. Her general health was good. There was nothing in the history to suggest a contact factor.

Physical examination in February 1940 showed hyperkeratosis and pigmentation on the knuckles, elbows, knees and achilles tendons. There was drying of the skin of the legs laterally, on the feet and to a lesser degree on the arms, with follicular keratotic lesions on the thighs laterally. On the dorsa of the hands, the arms and the mesial surface of the left thigh there was a hyperkeratotic, dully erythematous, scaling chronic eczematoid dermatitis. The skin was normal elsewhere. There was no atrophy of the tongue or glossitis. The knee-jerks were diminished. No muscular tenderness or increased capillary permeability was present.

After ten days of treatment with nicotinic acid amide (450 mg. per day), without local therapy or change in diet, the skin showed general improvement. She has been receiving 300 mg. of nicotinic acid amide since March 1.

Direct examination and cultures for fungus gave negative results.

DISCUSSION ON CASES OF VITAMIN DEFICIENCY

DR. GEORGE H. BELOTE, Ann Arbor, Mich.: These patients are presented not because all that is being said or written about vitamin deficiency is believed but because the internist is pointing out this or that type of cutaneous lesion as representative of vitamin A, B or C deficiency. Because of the pigmentation, the internist believes that the woman presented as having vitamin A and B deficiency also has C avitaminosis. This patient has been treated with nicotinic acid amide for three or four weeks, and the eruption, with no local therapy, has receded, I should say, by half.

The case of the other woman, who presented the red tongue and perlèche, raises the question of the causation of perlèche. It has been reported as due to this or that. Dr. Finnerud did some excellent work several years ago with *Monilia* cultures of material from lesions of patients with perlèche. Now the internists state that the condition is due to vitamin deficiency, not to infection. These cases were presented to find whether physicians in other parts of the country are thinking along the same lines.

DR. RICHARD S. WEISS, St. Louis: I wondered about the basal metabolic rate in the second case. The skin felt doughy and myxedematous. There have been cases of myxedema with scaliness of the skin. I wondered whether the patient had a low basal metabolic rate and whether she would have better results with thyroid medication.

DR. HERBERT RATTNER, Chicago: I thought the first case was a typical one of vitamin B deficiency. As to perlèche, there is a case at Michael Reese Hospital in which the condition responded to treatment with riboflavin, without topical treatment.

Gold Dermatitis and Stomatitis.

L. C., a white woman aged 46, has been treated in the arthritis unit of the department of internal medicine for chronic rheumatoid arthritis. Aside from the arthritis her past history revealed only occasional attacks of hives.

Between Aug. 24 and Nov. 27, 1939 she received weekly intramuscular injections of sodium gold thiomalate (myochrysine), totaling 1,010 mg. After each of the last three injections congestion of the conjunctiva, lacrimation and smarting of the eyes developed. Two weeks after the last injection an infection of the upper part of the respiratory tract and sore mouth developed. One month after the last injection she noticed scaling of the scalp, loss of hair and an eruption.

Examination on Jan 4, 1940 revealed a nonerythematous, patchy, dry, scaling eruption on the scalp, a papulosquamous eruption over the trunk and well defined erythematous, keratotic plaques on the palms. The buccal mucous membranes and lips revealed superficial small ulcers. The breath smelled foul and metallic. There has been gradual improvement to date.

A blood count on Jan 4, 1940 showed 80 per cent hemoglobin and 4,450 leukocytes per cubic millimeter, with a differential count of 77 per cent neutrophils, no basophils, 2 per cent eosinophils, 18 per cent lymphocytes and 3 per cent monocytes. There was no stippling of the erythrocytes, and the number of platelets was adequate. The urine was normal.

DISCUSSION

DR UDO J WILE, Ann Arbor, Mich. The department of medicine of the University Hospital has a substantial endowment for the study of arthritis. Large amounts of gold preparations have been given in the treatment of various arthropathies, and for this reason several cases of gold dermatitis have been observed. In some of these there is a striking resemblance of the eruption to pityriasis rosea. Dr Courville has been assigned to the study of this entity and will tell what he has found.

DR CHARLES J COURVILLE (by invitation), Ann Arbor, Mich. Gold compounds have been used for the past twenty years in the treatment of pulmonary tuberculosis, arthritis and lupus erythematosus. For the first two conditions large doses have been employed, varying between 100 and 500 mg. Of a series of 900 cases of arthritis treated with gold (Hartfall, S J, Garland, H G, and Goldie, W. *Lancet* 2 784 [Oct 2], 838 [Oct 9] 1937) 29 per cent had some type of cutaneous reaction. There is evidence to support the belief, as Dr Wile suggests, that the high incidence of toxic cutaneous manifestations in this group is due to the large dosage. The cutaneous reactions have been described by many observers as generalized pruritus, erythema, urticaria or a papular, squamous or eczematoid condition. More unusual forms are lesions suggesting lichen planus, giant urticaria, herpes simplex and herpes zoster. I have found reports of 2 cases in which the condition resembled pityriasis rosea. Stomatitis of varying degrees of severity has frequently been described.

I have recently observed 6 cases of dermatitis occurring during administration of gold sodium thiomalate for arthritis. In 2 of these there were eruptions similar to pityriasis rosea. The drug has been given cautiously, beginning with 10 mg and increasing to 100 mg, intramuscularly. The blood counts and results of urinalysis have been carefully watched.

The patients in whom toxic reactions developed have not all shown significant lowering of leukocytes. The leukocyte count of the patient presented on the day of her first injection of a gold compound was 4,800 per cubic millimeter. This fell to 3,600 per cubic millimeter after six weeks of treatment and fluctuated between this figure and 4,700.

At the onset of the first symptoms of intolerance to gold, the leukocyte count was 3,500 per cubic millimeter, the lowest noted, but it rose in spite of further gold therapy. The eruption appeared one month after her last injection. Perhaps this fall in the white cell count may be considered significant.

DR THEODORE CORNBLEET, Chicago. It would be interesting to examine the sections of the skin under the dark field to see if there are any deposits of gold.

DR CLARK W FINNERUD, Chicago. I should like to inquire whether any cases of gold reaction have been described in which there were seborrheic dermatitis-like or yeastlike forms of involvement of the angles of the mouth, nose or eyelids, or of the umbilicus, ears and scalp, with pseudoatrophy of and in the vicinity of the axillae. It should be easy to determine whether yeast is also etiologic in the stomatitis.

DR E A OLIVER, Chicago. I was surprised to find that Wise and Sulzberger, in "The 1939 Year Book of Dermatology and Syphilology," note that they believe that gold therapy should be superseded by the administration first of

a bismuth compound in all cases of discoid lupus erythematosus. They expressed the opinion that only in the cases in which all other treatment, including the bismuth therapy, had been given a fair trial and had failed is one warranted in administering a gold preparation.

DR. RICHARD S. WEISS, St. Louis: I have not had a great deal of experience with bismuth treatment, but in a small series of patients a few were apparently benefited. It seems to be similar in action to the gold therapy, but the results are not as good. I noted that this patient has had a consistently low leukocyte count. What constitutes a normal leukocyte count is a problem and a point of controversy among hematologists. There is apparently no normal value for any one person. It is exceedingly difficult to establish the base line. In the paper which Lane, Bagby and I presented (Weiss, R. S.; Lane, C. W., and Bagby, J. W.: *Effect on the Leukocytes of Therapy with a Gold Preparation*, ARCH. DERMAT. & SYPH. 35:1074 [June] 1937), we tried to do so, and we found from a study of hematologic literature that there were many opinions. We finally concluded that we would take the median rather than the "normal" from all the statements in the literature, and we chose 8,000. When a patient has a leukocyte count as low as 5,000 per cubic millimeter I feel that gold therapy is contraindicated and that it should be given with utmost caution. It has been my experience that a patient who starts treatment with a low leukocyte count tolerates gold poorly. I should not say that the patient under consideration tolerated gold poorly; she appeared to be getting a large dose. It is my feeling that when the leukocyte count is low the patient is much more apt to have a reaction, and therefore some other method of treatment should be used.

DR. HERBERT RATTNER, Chicago: I have observed in the same person a pityriasis-rosea-like eruption during the course of treatment with gold and again during treatment with bismuth.

DR. OTTO FOERSTER, Milwaukee: This represents a new type of dermatitis due to gold. The usual feature of hemorrhages in the gums indicates again that gold is toxic for endothelial cells.

Localized Amyloidosis of the Legs. Presented by DR. UDO J. WILE, Ann Arbor, Mich., and DR. A. E. SCHILLER, Detroit.

L. B., a man aged 45, noted a pruritic patch on the lower part of his right leg in the summer of 1938, which disappeared with exposure to the sun during the summer. After his fifth operation on the stomach since 1922 (resection in October 1938), the eruption reappeared, involving almost the entire leg. This again disappeared during the summer of 1939, only to recur with bilateral involvement in the fall. An intradermal test with congo red, performed at Grace Hospital, Detroit, two weeks ago, caused redness of the papules in that area. He has complained of a pruritic papular eruption on the arms, axillas, trunk and inguinal region since beginning to take nicotinic acid three months ago. The patient has two unrelated cutaneous conditions, but he is being presented only for consideration of the eruption on the legs. The skin of the legs is thickened, firm and studded with many pinhead-sized to glass pinhead-sized, flesh-colored papules, some of which are covered with a fine, tightly adherent scale. The papules are discrete, but are grouped in some areas. In addition, there is a generalized pigmented papular and excoriated eruption involving the arms, axillas, trunk, buttocks and inguinal region. The Kahn reaction of the blood was negative.

Localized Amyloidosis of the Tongue, Pharynx and Eyelids.

N. H., a white man aged 62, gives a history of attacks of sore tongue and sore throat since the age of 20. These would clear up with local treatment alone, only to recur within six months to a year. The condition had been diagnosed as syphilis, and he had received a few injections of arsphenamine, without improvement.

He was first seen at the University Hospital in 1919, at the age of 42. A clinical diagnosis of syphilitic glossitis was made, although the results of serologic examination were negative. The patient was given antisyphilitic therapy at the outset, and the ulcers on the tongue and pharynx healed. During the next three years he received a total of sixteen intravenous injections of arsphenamine, several full courses of mercury rubs and a large amount of potassium iodide. The serologic reactions remained negative, although new crops of ulcers appeared. In 1925 the patient had an attack of "yellow jaundice."

In 1931 he returned with another attack of "sore tongue." At this time he presented involvement of the hard and soft palate, and around the ulcers on the tongue were seen for the first time small yellowish nodules. Histologic examination showed an inflammatory papilloma containing much hyaline material, apparently resulting from hyaline changes in vessel walls. At this time he also presented numerous small nodules on the eyelids. From 1931 to 1934 he received twenty-seven intramuscular injections of bismuth subsalicylate, 2 grams (0.13 Gm.), together with potassium iodide, with no appreciable effect on the lesions.

At present the patient presents diffuse involvement of the tongue, hard and soft palate, pharynx and larynx. This is nodular and is definitely yellow. A destructive lesion is present in the left tonsillar region. Small nodules are also present along the margins of the lid. The patient also presents dry, atrophic skin of the hands, face and ears.

Numerous Kahn reactions of the blood have all been negative.

DISCUSSION ON CASES OF LOCALIZED AMYLOIDOSIS

DR UDO J. WILE, Ann Arbor, Mich. The lesions in the mouth of this patient were at one time ulcerated, and, notwithstanding the negative serologic reaction, he was treated for gumma of the tongue. While the lesions in the mouth and on the tongue are hard and boardlike, as in amyloid diseases, the lesions on the elbows, knees and eyelids do not in any way resemble other known examples of cutaneous amyloidosis.

A Case for Diagnosis (Erythema Figuratum Perstans?)

H. M., a girl aged 17, was previously presented before the Detroit Dermatological Society in April 1939 (Wile, Udo J., and Belote, G. H. A Case for Diagnosis, *ARCH. DERMAT. & SYPH.* 40: 681 [Oct.] 1939).

DISCUSSION

DR FRANCIS E. SENEAR, Chicago. I do not believe that this case can be classified as one of erythema perstans. First, the lesions are much larger than those usually seen in that disease. Second, each one of the lesions has increased in size slowly, and none of them has shown any tendency to disappear. The lesions of erythema centrifugum individually run a much slower course. Third, there is a considerable amount of crusting and scaling about the margins of these lesions, and this element is entirely lacking in the description of erythema perstans by Darier. It is true that Gougerot has described cases in which there were scaling and even vesiculation at the periphery, but certainly not to the extent to which it is present here.

While I am not at all certain as to the diagnosis, I think that a superficial type of late syphilis must be considered. The patient states that the lesions itch, but this is minimal and intermittent. The only other possibility that occurs to me is that the condition might be an annular type of psoriasis.

DR GEORGE H. BELOTE, Ann Arbor, Mich. The serologic reaction was negative six months ago. At the time this patient was presented last year she had been seen earlier by one of the members, who thought the condition looked like pityriasis rosea. When I saw her at the meeting in Detroit the condition looked like atypical psoriasis. It has taken on certain features which are unusual for psoriasis. At present I admit that I am not fully convinced what this condition is, I do not believe it is syphilis. As a matter of fact, active syphilis

in patients with negative Wassermann reactions are rarely seen in this hospital. I am not certain whether the condition is atypical psoriasis, as Dr. Senear has suggested, and am not at all convinced that it does not belong in the group of annular psoriasis, where it was placed tentatively.

A Case for Diagnosis (Pruritic Melanoderma of Undetermined Origin).

Presented by DR. H. J. PARKHURST, Toledo, Ohio.

A. D., a man aged 68, has lived alone in a cabin and subsisted on relief provisions and on what he has earned by doing occasional gardening and odd jobs. Aside from the diseases of childhood, he has had no illnesses, except asthma of undetermined origin, which had been present at all seasons since he was 10 years old. Cutaneous tests with foods and grasses have given negative reactions. For the last eight years, in order to relieve the asthma, he has smoked mullein (*Verbascum thapsus*) and jimson weed (*Datura stramonium*) and the mixture several times every day. For at least three years there has been severe itching of the face, ears, neck, hands, lower portions of the arms and the forearms; at times the ankles and other areas have also been involved. The exposed surfaces have become moderately lichenified and dark brown. This condition was fairly sharply limited to the areas mentioned, the rest of the cutaneous surface being of the moderately dry senile type, with moderate senile hyperpigmentation in the usual locations. The upper third of each ear was considerably thickened. Inside the left cheek, in the molar area, there was a fairly well outlined, pea-sized, slate-colored macule. There was no glossitis. There was slight enlargement of some of the cervical, axillary and inguinal lymph nodes, but this was not pronounced. The physical examination revealed nothing noteworthy, and the spleen was apparently not enlarged. The blood pressure was 140 systolic and 90 diastolic in 1937, 138 and 75 in 1938 and 120 and 70 in 1939. There has been little impairment of physical strength. The urine has shown no abnormality. The blood count per cubic millimeter, with a hemoglobin percentage of about 4,000,000 erythrocytes, 8,000 and 9,500 per cubic millimeter. The proportions of the white cells were normal except for constant moderate eosinophilia (from 3 to 16 per cent between phils and, more recently, from 4 to 8 per cent). The Wassermann reaction was repeatedly negative.

In October 1939 skin from the forearm and an inguinal lymph node were removed for histologic study. Dr. T. L. Ramsey gave the following report: "In the sections of skin the epidermis was somewhat thinned but moderately hyperkeratotic. There were granules of pigment in the upper part of the derma which gave a positive dopa reaction. There was definite infiltration of reticulo-histiocytes in the upper part of the derma and the papillae, especially perivascular, with some edema. In the lymph node the normal glandular architecture seemed somewhat distorted. There were diffuse edema and considerable interstitial fibrosis; the germinal centers appeared indistinct, and there was a definite increase in the reticulum. There appeared to be a marked increase in large cells of the endothelial type, and many large mononuclear cells were present. Some areas showed proliferation and infiltration with fibroblasts. Granules of brownish pigment were scattered throughout the reticulum which gave a positive dopa reaction. There was a definite increase in thickness of the fibrous capsule." Dr. S. W. Becker, of Chicago, gave this report: "We have studied the sections . . . and believe that they can be interpreted as follows: The patient evidently has a generalized pigmentary disease which cannot be classified with any of the common melanotic eruptions. Owing perhaps to coexisting dermatoses, the melanin has been absorbed in the lymph and is deposited in histiocytes in the dermis. There is also some melanin in histiocytes in the lymph nodes. I believe that this large number of histiocytes, or reticuloendothelial cells, has been evoked merely to take care of the excess of melanin and cannot be considered as a primary change."

During the past three years the patient has spent several months in the hospital at various times, and diagnoses of pellagra, Addison's disease, photosensitization and benign hyperplastic cutaneous reticulohistiocytosis with melano-derma (Baccaredda) have been considered and excluded by therapeutic tests and observation. The following theory is now tentatively presented. Mullein is known to be a rubefacient, and the patient's skin reacts positively to it in patch tests, as would be expected. His face, neck, hands and forearms are especially exposed to it when he is at home. When jimson weed is smoked, the nervous system is affected as by atropine, and the cutaneous innervation is included, with a possible effect on the formation of pigment. Perhaps this might explain the localized pigmentation and histiocytic reaction in areas irritated by mullein.

DISCUSSION

DR HARRY R FOERSTER, Milwaukee. A photosensitization reaction is suggested by the intensity of the pigmentation on exposed parts. The pigmentation on the covered parts is moderate and may be due to senility and vagabondism. The absence of pruritus and of chronic infiltrated dermatitis in the exposed areas of the forearms, hands, neck and face is against a diagnosis of allergic sensitization. Addison's disease has been ruled out, and if the condition were a pellagrous manifestation due to a vitamin deficiency, this would probably have been disclosed during his period of hospitalization. It is known that the ingestion of certain plants may produce photosensitization in domestic animals. May not the condition in this case be a similar type of photosensitization through swallowing juice of the weed mixture which was smoked?

NOTE—It was later suggested to Dr Parkhurst that the patient's living environment made photosensitization from coal dust a possibility.

DR H J PARKHURST, Toledo, Ohio. I had considered the possibility of photosensitization but felt that it was excluded because of the fact that the patient had received generalized ultraviolet radiation for some time, without apparent aggravation of the cutaneous condition. Prolonged treatment in the hospital seemed to exclude the possibility of vitamin deficiency as an etiologic factor.

 NEW YORK DERMATOLOGICAL SOCIETY

FRANK C COMBES, M D, *President*

J GARDNER HOPKINS, M D, *Secretary*

March 26, 1940

A Case for Diagnosis (Mikulicz' Disease?) Presented by DR GEORGE M MACKEE

Miss F D, a stenographer aged 35, a private patient, gives a rather irrelevant past history. She had a gallbladder operation and an appendectomy in 1923. She is of somewhat nervous temperament. The menses have always been regular but exceedingly scanty, lasting only an hour or two. In May 1939 her friends called her attention to a swelling of the cheeks. This was not preceded by or associated with any illness. There has been a slow, progressive increase in the swelling. At times the swelling is worse than at other times, but there have been no definite exacerbations and remissions. There has been no evidence of inflammation, such as heat or redness, and there has been no fever. There has been no difficulty in opening the mouth. There has been no hyperesthesia, hypoaesthesia or perceptible change in the salivary secretion. The patient has neither gained nor lost weight. She received from other physicians injections of various kinds, probably for the scanty menses. These injections had no apparent effect on the swelling of the cheeks. At one time the swelling was aspirated, probably because

the physician thought there was a cyst. No fluid was obtained. Two roentgen ray treatments had been given at weekly intervals, each treatment consisting of $\frac{1}{4}$ erythema dose, the filtration being 3 mm. of aluminum. The treatment was discontinued because of lack of confidence.

The patient presents a poorly outlined, boggy swelling of the cheeks about the size of a palm. The edges of the swelling are perceptible by palpation. The mass lies over the ascending ramus of the jaw down to the mandible, extending upward in front of the ear and forward to about the center of the cheek. There is no visible evidence of inflammation. There is absolute symmetry, even to a dimple or dell in the center of the mass. There is no pitting on pressure. The skin overlying the tumors has a normal appearance. The interior of the mouth is normal. The swellings give to the patient a peculiar appearance. The jowls look heavy. The swellings have, perhaps, a thickness of 1 cm.

The diagnoses that have been considered are: some form of lipodystrophy, panniculitis, angioneurotic edema, dermatomyositis and particularly some chronic condition of the parotid glands.

DISCUSSION

DR. EUGENE F. TRAUB: If this involvement is of the parotid gland, and there seems to be some question as to where these boggy swellings actually lie, I think it is an example of Mikulicz' disease, of which I have encountered 1 or 2 cases. It is most easily recognized, of course, when there is bilateral involvement of the lacrimal glands as well as of the parotids, and frequently the submental glands are also involved. Here there is involvement only of the parotid glands—if the swelling is in the parotid glands and not in the skin or subcutaneous tissue.

DR. GEORGE C. ANDREWS: I am inclined to agree with the diagnosis of panniculitis.

DR. J. GARDNER HOPKINS: It seems to me that the lesion is in the skin or attached to the skin. The skin does not move over the lesion as it would if it were in the parotid gland. The presenter has suggested all the possibilities. There is some resemblance to the case recently presented by Dr. Andrews of panniculitis following lupus erythematosus (ARCH. DERMAT. & SYPH. 41:965 [May] 1940). Some form of lipodystrophy seems the most likely diagnosis.

DR. PAUL E. BECHET: The two indurated areas are symmetric and even uniform in size. Even the dimpling is exactly similar in location on the two sides. It seems to me that this should constitute presumptive evidence that the parotid glands are affected.

DR. EDWARD R. MALONEY: I agree with Dr. Hopkins. The lesions seem to be in the skin or subcutaneous tissue, and there is no evidence that any glands, the parotid or any other, are involved. In spite of the fact that there is no history of attacks of erysipelas, it seems to me that a good clinical diagnosis would be solid edema, which is a diagnosis which Dr. MacKee has also considered. I should make that diagnosis in this case.

DR. J. FRANK FRASER: I agree with Dr. Maloney's view that this case is one of solid edema. One cannot be sure of the causative factors. If the parotid glands were involved one should expect more swelling under the mandible and beneath and behind the ear. A biopsy of deep tissue might be helpful.

DR. R. H. RULISON: I think the condition is in the skin or subcutaneous tissue and not in the gland. In my opinion the diagnosis of sclerema or scleroderma is the most likely one.

DR. A. BENSON CANNON: If the duct were functioning normally, could one not inject a dye into it and take a roentgenogram to see if the swelling is not really in the glandular tissue?

DR. FRANK C. COMBES: I doubt that the condition involves the parotid glands, in spite of its absolute symmetry. I have had 2 cases in which I made a diagnosis of Mikulicz' disease, 1 with a tumor on one side and the other with tumors on both sides. In 1 case I gave two treatments with roentgen rays, giving $\frac{1}{2}$ erythema dose, well filtered. There was no improvement at the end of two months. I sent the patient to a surgeon, who made an incision and found

at the facial nerve went through the gland. He closed the wound without using anything. In the course of the next two months the condition cleared up entirely. The tumors were bilateral in the other case. I gave two suberythemas of roentgen rays, and outside of a little dryness of the mouth, which lasted about two months, the lesions cleared up entirely. In the first case I mentioned, the tumor was hard and shotty, much like a cyst, in fact, I tried to incise it, without success. In the second case the tumor was found beneath the mandible and all the way up the side of the face. At the same time the patient complained of pain in the back of the neck. When the parotid gland enlarges, of course, it is likely to change its anatomic position.

DR GEORGE C ANDREWS Did the patient of Dr. Combes exhibit dryness of the mouth before treatment? Dryness of the mouth, of course, is a symptom of the disease. Did the treatment relieve it?

DR FRANK C COMBES No. The dryness of the mouth was not present before but occurred only after the treatment with roentgen rays.

DR EDWARD R MALONEY Mikulicz' disease is more common among negroes.

DR GEORGE M MACKEE The diagnosis is difficult, and also it is difficult to determine the anatomic position of the condition. The perfect symmetry and relation to the position of the parotid glands strongly suggest a parotitis of some kind, possibly Mikulicz' disease, a condition with which I am unfamiliar. The fact that the skin and the subcutaneous tissue appear to be involved may indicate solid edema or some form of lipodystrophy, unless the inflammation of the parotid glands has spread to the overlying tissue.

Articulated Pigmented Poikiloderma of Civatte Presented by DR GEORGE C ANDREWS

Mrs. L. M., aged 46, first noticed lesions about the neck, in the upper sternal region and on the back in January 1939 after wearing a new black fur collar. There was some redness and itching of the lesions at first, but now she notices only a burning sensation when clothing of any type touches the neck. The patient's general health has been good, and there have been no past illnesses of significance. Her menses stopped in November 1939.

The eruption consists of a network of pigmented and atrophic spots rather symmetrically arranged on the neck and sides of the face. The lesions are macular and reddish brown, with a tendency at times to scale and show angiectasia.

Treatment has consisted of six doses of 10,000 units of estrone (theelin), five treatments of 50 r each of unfiltered roentgen rays to the affected parts and no external medication. This treatment has apparently diminished the subjective symptoms but has had no influence on the appearance of the lesions.

DISCUSSION

DR J. FRANK FRASER I agree with the diagnosis as presented.

DR EUGENE F. TRAUB I do not wish to disagree with the diagnosis as presented, but conditions like this are seen often in many persons on the exposed area of the neck and chest. In addition, in this particular case I did not see any annular lesions or tiny papules, which are supposed to occur occasionally with this condition. There are no white spots and no special configuration. I should like to know, therefore, how one can say that this case is one of poikiloderma when there are many women, particularly those who wear V-necked dresses, who present this type of change in the skin? I should like to ask whether there is any way of telling when one has poikiloderma of Civatte and when one has not.

DR PAUL E. BECHET I have always been interested in dermatoses in which ultraviolet light might play an etiologic role. Is Civatte's disease a member of this group? Or can it be attributed to endocrine dysfunction? The points in favor of the latter are few. They rest on its predominance in women, particularly at the menopause, its occasional tendency to regress under the influence of hor-

monal therapy and the presence of telangiectasia. On the other hand, the evidence that Civatte's disease is due either to hypersensitivity to light or to overexposure to light is, in my opinion, overwhelming. Telangiectasia can be caused by overexposure to light. It is a common occurrence on the faces of sailors and farmers. If Civatte's poikiloderma is not due to actinic light, why does it almost always occur on the face and neck, areas of the body which are most frequently exposed to the sun? I have often observed fishermen, sailors and farmers with reticulated pigmented telangiectatic patches on the neck identical with areas of Civatte's disease. If Civatte's disease is not an actinic dermatitis, why is it classed in a number of textbooks as a synonym of Riehl's melanosis? Despite the fact that Dr. Andrews' patient says that she has never been exposed unduly to sunlight, I have observed large lentigenes on the upper part of her back. She has, besides, pearl white skin, which is usually sensitive to light.

DR. GEORGE M. MACKEE: I agree with the diagnosis. Mild attacks of the disease are common in women. Usually the condition is limited to the sides of the neck, but occasionally it may involve the entire face, neck and a portion of the chest, even parts that are seldom, if ever, exposed to direct or indirect sunlight. It may or may not be accompanied by "farmer's skin," and it may be mistaken for "farmer's skin." As I know the disease, it consists of yellowish brown pigmentation with more or less telangiectasia and some atrophy. The color varies somewhat in accordance with the relative amounts of pigment, telangiectasia and atrophy. The cause may be exposure to the sun's rays, but this has not been proved. I have always regarded this progressive condition as an entity.

DR. EDWARD R. MALONEY: I think there may possibly be something in what Dr. Bechet has said about hypersensitivity to light in these cases, but I think there is something more than that. Most patients with this condition have avitaminosis too and should be studied from that point of view also. The eruption is somewhat analogous to the eruption seen in patients with pellagra. I think avitaminosis is at the basis of this condition, and hypersensitivity to light may have something to do with it.

DR. EUGENE F. TRAUB: According to most of the textbooks, for instance the one by Sutton, melanosis of Riehl is included as being the same process as poikiloderma of Civatte. The original description given by Civatte (*Ann. de dermat. et syph.* 4:605, 1923) portrayed lesions which began on the forehead and spread down on the cheeks. The region about the eyes and mouth remained clear. Later the lesions extended down on the neck and in some cases down on the arms. Civatte described the reticulated appearance of the skin with small erythematous patches varying up to 1 cm. in size. The areas underwent atrophy with some pigmentation. Some telangiectasia appeared in the areas. Graham Little more recently reported a series of cases in which with a single exception the condition occurred in women, especially those of menopausal age. In these patients the eruption was distributed over the face, the neck and the upper portion of the chest and shoulders. In his opinion if there was any one feature that might be designated as characteristic, it was the reticular network consisting of tiny inflammatory papules covered with a little scale. Some of the patients presented white spots, while others showed considerable pigmentation. Areas of telangiectasia and atrophy were present in a number of cases. While not all of these symptoms are necessarily present in every case, most of the patients present a fair number of these features.

DR. GEORGE C. ANDREWS: Why does Dr. Traub think this case does not fit in with that description?

DR. EUGENE F. TRAUB: In this case I did not see any tiny papules, scaling or evidence of an erythematous eruption, and I was not at all certain of the presence of atrophy, real reticulation or white spots, such as I have just mentioned as having been described by Civatte.

DR. GEORGE M. MACKEE: I have never seen desquamation in cases of this disease.

DR GEORGE C ANDREWS (by invitation) In bright daylight I examined this patient closely and studied the condition. She shows reticulated lesions in well defined patches in normal skin. That, it seems to me, would tend to rule out actinic dermatitis. The patches themselves consist of brownish pigmentation and definite white patches of distinct atrophy. There are areas of telangiectasia, and some of the erythematous spots are a little scaly, although scaling is insignificant. To my mind this is the most striking and definite example of poikiloderma of Civatte I have ever seen. The age of the patient and the character and progression of the lesions are characteristic. As Dr MacKee said, I never heard of the papules and annular lesions mentioned by Dr Traub. I believe poikiloderma of Civatte is a definite entity. I think it is an idiopathic atrophy of the skin. I questioned this patient about vitamins. She has a good appetite and eats liberally. There is no sign of a vitamin deficiency. The tongue is not glazed. She has no anemia. She gives no history of exposure to strong sunlight. She leads a sedentary indoor life.

DR GEORGE M MACKEE There seems to be a difference of opinion as to just what constitutes this disease. Dr Traub has just read a description of it from Sutton's book. I do not agree with that account. Riehl's melanosis was mentioned in that description as being identical with poikiloderma of Civatte. That certainly is not my conception. Riehl's melanosis consists simply of pigmentation, with no atrophy or telangiectasia. I agree with Dr Andrews that this case is a typical one of poikiloderma of Civatte, although the condition is unusually extensive.

DR EUGENE F TRAUB I mentioned Civatte's original description and the case reports of Graham Little, which I investigated some time ago simply because the features stressed by these two authors as being so characteristic and essential did not seem to me to be characteristically present in this case.

DR EDWARD R MALONEY I agree with the clinical diagnosis as presented.

DR GEORGE C ANDREWS I feel as Dr MacKee does, that Riehl's melanosis is an entirely different picture, with a different distribution and different course.

DR FRANK C COMBES I think that Riehl was the one who made the statement that the cases of poikiloderma of Civatte were the same as his. I imagine myself that the two conditions are distinct. Riehl considered that the condition in his original cases was identical with that in those later described by Civatte.

Acne Aggregata seu Conglobata Presented by DR PAUL E BECHT

S S, a girl aged 10 years, was brought by her mother to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital today. She presented innumerable comedos and double comedos, papules and pustules and follicular and perifollicular inflammatory infiltrations, covering most of the cheeks and forehead. The scarring is extremely severe and consists of depressed, reddened, crateriform cicatrices varying from 0.5 to 1 mm in diameter. The eruption has been present for one year. The child is thin, pale and emaciated and seems to be in poor health. The case is presented because of the unusual severity of acne, with extensive scarring and resulting disfigurement, beginning at the age of 10 years.

DISCUSSION

DR EDWARD R MALONEY This case seems to me to be a typical one of acne pustulosa or acne vulgaris. I do not see why such a lengthy name was given to it. I should call it a case of acne vulgaris in a young girl. Ten years of age is young for this condition.

DR R H RULISON I thought the condition was precocious acne.

DR GEORGE M MACKEE I agree with Dr Maloney that this case is one of severe acne vulgaris or acne indurata, which are the same thing. I do not think the condition is severe enough to be called acne conglobata or the pyoderma faciei of O'Leary.

DR. FRANK C. COMBES: I agree with the previous speakers.

DR. PAUL E. BECHET: In presenting this patient with a diagnosis of acne aggregata seu conglobata, I had no idea of confusing the members of this society with a new and long name or pretending that the condition was a rare type of acne. The term was used by Ormsby (Ormsby, O. S.: Diseases of the Skin, ed. 5, Philadelphia, Lea & Febiger, 1937, p. 1184) to describe an acne characterized in its early stages by the presence of innumerable comedos and double comedos, papules and pustules and follicular inflammatory infiltrations, with resulting extremely severe variola-like scars. In the later stages of this disease, large indolent sebaceous, multilocular abscesses and large dusky red, elevated, fluctuating plaques with enormous scarring, at times keloid-like in character, occur. My only reason for the presentation is the age of the patient and the severity of the condition at such an early stage. Allowed to remain untreated, such an acne can result in permanent and extensive disfigurement. In my experience it almost always occurs in anemic, cachectic, emaciated, "run down" persons usually of the pre-adolescent or adolescent age. In my opinion it is a clinical entity and is not an exaggerated form of indurated acne, nor is it tuberculous or tuberculoid. The foregoing description exactly fits the clinical picture exhibited by this girl.

A Case for Diagnosis (Seborrheic Dermatitis? Parapsoriasis? Cutaneous Manifestation of an Endocrine Dysfunction?). Presented by DR. PAUL E. BECHET.

E. M., a girl aged 4 years, was brought by her mother to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital for the relief of an extensive eruption on the upper eyelids and on the angles of the chin, arms, trunk and legs. The mother states that the eruption has been present for two years. The lesions consist of erythematous, scaly, plaquelike, irregular but sharply margined patches. On the trunk some of the patches consist of grouped, exceedingly small hyperkeratotic lesions. They are definitely not confluent, and the intervening skin is normal in appearance. The child is much overweight. She has the characteristic moonlike face and the usual distribution of fat so frequently observed in persons with dystrophia adiposogenitalis. There is no history of ingestion of drugs. The histologic observations were not significant.

DISCUSSION

DR. GEORGE M. MACKEE: I will make a tentative diagnosis of eczema of unknown variety and of unknown cause, because of the patches of eczematoid dermatitis and because of the follicular element on the abdomen. I also am thinking of the possibility of parapsoriasis or even of an aberrant psoriasis.

DR. EUGENE F. TRAUB: It seems to me that this girl has unusually dry skin in general, with certainly an exaggerated keratosis pilaris or something akin to that. I wonder if some of those follicular keratotic plugs are not due to congenital dryness of the skin, as seen in mild xeroderma with associated keratosis pilaris, which perhaps may account for the fact that the lesions are so dry and scaly. In addition, she may have an eczema which because of the excessively dry skin assumes this peculiar picture. The only other diagnostic possibility that suggests itself to me, and that because of the peculiar lesions on the chin and around the mouth, is that this condition is psoriasis, which at the present time is atypical.

DR. EDWARD R. MALONEY: Dr. MacKee has expressed in a much better way than I could have myself my opinion in this case.

DR. J. FRANK FRASER: Dr. Traub has mentioned keratosis pilaris. This condition may accompany other dermatoses. The history of two years' duration, with disappearance in the summer, and the appearance of the lesions, especially those adjoining the mucous membranes, with well demarcated borders suggest the diagnosis of an aberrant psoriasis. On the other hand, the involvement of the commissures points to the possibility of a fungous infection, possibly moniliasis. I should like to ask whether any mycologic study has been made.

DR R H RULISON Dr Fraser has said almost everything I had in mind about this case. I think that the most likely diagnosis is moniliasis, and my next choice would be psoriasis.

DR FRANK C COMBES My interpretation of this case is more in agreement with what Dr Traub has said. According to the history I received from the child's mother, these patches of keratosis pilaris on the abdomen are of more recent occurrence. The patches that are more acutely inflamed appeared similar to those on the abdomen now, and after the application of various salves they assumed their present appearance. I do not agree that this condition is Frohlich's syndrome, the patient is too young for that, but I think there is a strong probability that she has hypothyroidism, which would account for the dryness of the skin and for the keratosis pilaris. Skins like this are prone to eczematous reactions, particularly in cold weather. In the summer, I understand, these lesions disappear entirely. Of course, psoriasis in most cases also has a tendency to disappear in the summer on exposure to the sun. These patches do not have the distribution or appearance of psoriasis. They seem to be deeper than what one expects in psoriasis, and there is a suggestion of a crust on the lesions rather than a scale. Although I can see no evidence of vesiculation and the patient did not complain of any itching, the condition seems to me like chronic or subacute dermatitis or eczema.

DR PAUL E BECHET I had the same difficulty in making a diagnosis as that of most of the members. I did not consider moniliasis. My impression in reference to Frohlich's syndrome differs from that of Dr Combes. I will grant that the patient (4 years old) is possibly too young to show signs of pituitary dysfunction. On the other hand, I have seen typical dystrophia adiposogenitalis at the age of 10 or 13 years, with a history of the onset of the disease five or six years previously. The patient under discussion has the moon face and the usual distribution of fat of Frohlich's syndrome. The fat is precocious, and the condition does not resemble the usual picture of an obese child. In my opinion it is not possible to make a definite diagnosis without further investigation. On the other hand, I have noticed, oddly enough, in several instances of Frohlich's syndrome in preadolescent children the same follicular keratosis which this little girl presents on her abdomen. This follicular keratosis resembles the early lesions of pityriasis rubra pilaris. One of my patients, a boy aged 13, with definite pityriasis rubra pilaris and well advanced dystrophia adiposogenitalis, was given $\frac{1}{2}$ grain (0.03 Gm) of posterior pituitary three times daily. There was decided improvement in both the eruption and the hypopituitary condition within a few weeks. I feel that it might be possible that the keratotic lesions on this patient's abdomen are related to hypofunction of the hypophysis cerebri.

Panniculitis Following Lupus Erythematosus Presented by DR GEORGE C ANDREWS

W L, a woman aged 29, was presented before this society on Dec 19, 1939 (*ARCH DERMAT & SYPH* 41 965 [May] 1940).

Since the presentation of the patient, I have reviewed the histologic section and made further search for actinomyces. There have been cultures and direct smears, which have been negative. The histologic section showed nothing except signs of an inflammatory condition in the fat. Clinically the condition is unchanged. Fractional roentgenotherapy to the infiltrated area has been started just recently.

Epidermolysis Bullosa Acquisita Presented by DR PAUL E BECHET

L M, a woman aged 43, was presented before this society on Jan 23, 1940 (*ARCH DERMAT & SYPH* 42 210 [July] 1940).

When this case was presented, a diagnosis of dermatitis herpetiformis was made by some of the members. The histologic examination showed the characteristic lesions of epidermolysis bullosa with loss of elastic tissue on special

stains. The patient still attends the clinic and constantly shows lesions acquired through trauma. She went bowling one evening and the next day had two large bullae on the index finger and thumb from pressure of the ball. I believe that this case is a bona fide one of epidermolysis bullosa of the acquired type. The patient has been given chorionic gonadotropin (antuitrin S) and is showing some improvement.

DISCUSSION

DR. GEORGE M. MACKEE: In support of Dr. Bechet, I will say that I have seen the patient two or three times since her presentation here, and I can verify the fact that the lesions certainly are on the areas which are frequently traumatized, and they apparently do not occur spontaneously but only as a result of trauma. I finally came to the conclusion that Dr. Bechet was correct in calling this condition epidermolysis bullosa acquisita.

 PHILADELPHIA DERMATOLOGICAL SOCIETY

J. V. KLAUDER, M.D., *Chairman*

HERMAN BEERMAN, M.D., *Secretary*

April 19, 1940

"Open Bite" in Association with Prenatal Syphilis. Presented by
DR. BERTRAM SHAFFER.

C. J. S., a healthy Negro boy aged 12 years, has a somewhat suggestive facies, bilateral palpable epitrochlear lymph nodes, an external squint of the left eye, hutchinsonian incisors and the peculiar dental deformity for which he is presented. The anterior part of the upper dental arch is raised, so that it is impossible to bring the upper and lower incisors into approximation. A diagnosis of congenital syphilis was made on Dec. 31, 1927, because of a positive serologic reaction of the blood and roentgenographic evidence in the long bones. He was treated until 1933, with thirty-three injections of sulfarsphenamine and forty-four injections of bismuth and potassium tartrate. Examination of the cerebrospinal fluid on Jan. 23, 1940 gave negative reactions.

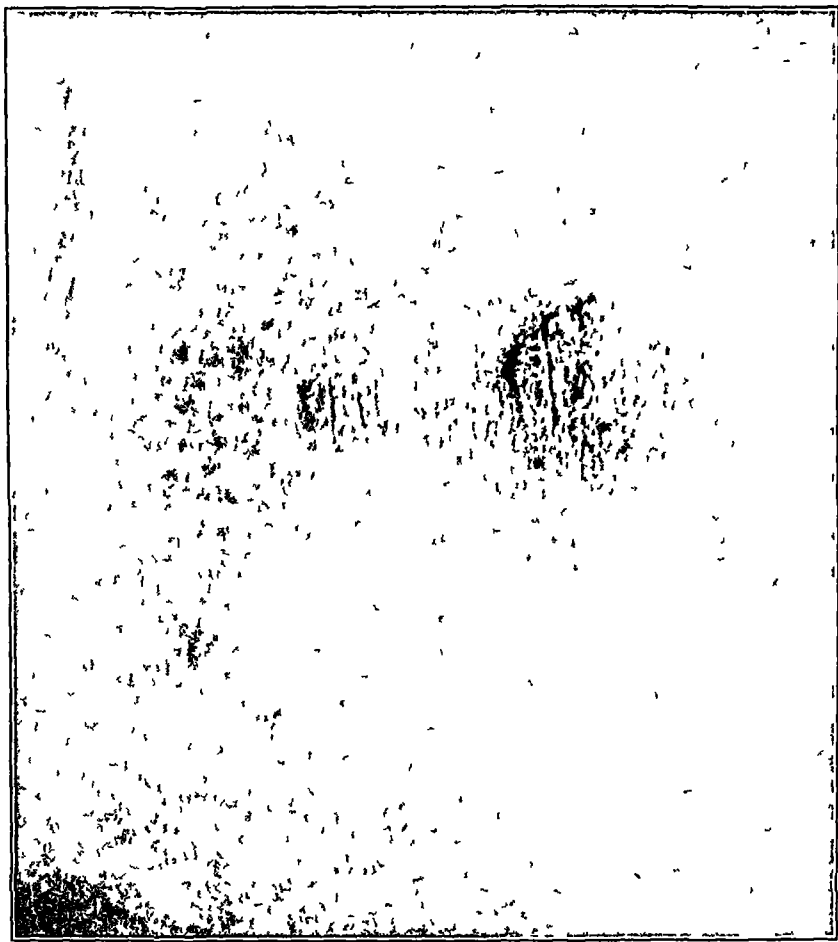
DISCUSSION

DR. J. V. KLAUDER: The "open bite" is, I believe, the least mentioned of the three most significant dental findings that characterize congenital syphilis, the others being hutchinsonian teeth and Moon's, or mulberry, molars. It is interesting to note that Moon, who described mulberry molars, lived at the time of Hutchinson and was a dentist at one of the London hospitals. I do not think that the "open bite" is diagnostic of syphilis, but it is infrequent in patients who do not have congenital syphilis. This patient does not have other stigmas of congenital syphilis that are usually dealt with in textbooks, such as Clutton's joints and peripheral choroiditis. I believe that dermatologists should think in terms of the ectoderm and examine the eyegrounds of patients with cutaneous disorders.

DR. JOHN H. STOKES: I recognized the example of this stigma that Dr. Klauder has so wisely emphasized. I suggested that Dr. Shaffer look into the French literature on the anomalies of development of the center of the face. These affect the upper central incisors and the arch of the palate and cause the "dishing" of the face, as it is sometimes called, and the flattening of the nasal bridge which has no connection with any injury to or destruction of the septum. Several French writers have insisted that the effect of the toxin of *Spirochaeta pallida* on the embryo is the cause of a good deal of the diagnostic facies and other important stigmas in the person with congenital syphilis.

Psoriasis Associated with Lichen-Spinulosus-like Eruption Presented by
DR DONALD M PILLSBURY and DR BERTRAM SHAFFER

D C, a white girl aged 5 years, rather obese but intelligent, presents on the anterior parts of the legs diffuse patches of closely set hyperkeratotic follicular lesions with pronounced spine formation. On the right arm there is a sharply circumscribed group of lesions of similar nature. There are many discrete and confluent psoriasiform lesions in the same sites. "Rough areas" developed on the extremities about fifteen months ago. Three months later "red scaling spots" appeared, following the scratching and picking of the earlier lesions. The results of



Psoriasis associated with lichen-spinulosus-like lesions

medical examination were negative. A complete blood count was normal. The tuberculin test, with a 1:1,000,000 dilution of old tuberculin, gave a negative reaction.

DISCUSSION

DR BERTRAM SHAFFER: I should like to know what the members think of the follicular lesions. Curiously, they preceded the psoriatic lesions. The psoriatic lesions occurred in the patches of lichen-spinulosus-like lesions after the child traumatized them because of pruritus. I wonder if this condition could be a Kobner-like reaction.

DR SIGMUND S GREENBAUM: Histologic examination of one lesion would settle that.

DR. JOHN H. STOKES: In considering clinical pictures like this one ought also to think of some of the anomalous rare types of Devergie's disease. In them are seen follicular eruptions which are not characteristically on the dorsa of the fingers and the forearms, and early in the course of the process psoriasiform changes ensue. It is well also to keep in mind the follicular "ids," both tuberculids and dermatophytids, and a careful search ought to be made for any evidence of a fungous infection. I remember, to my chagrin, a child who had what I thought was atypical Devergie's disease. She went to Chicago, and Dr. Fred Harris showed the cultures of favus from her finger nails. One has to be extremely careful to eliminate fungous infections in situations of this sort. The scalp should be searched with the utmost care.

A Case for Diagnosis (Squamous Cell Carcinoma in Scar of Lupus Vulgaris After Trauma?). Presented by DR. DONALD M. PILLSBURY.

L. L., an asthenic, pale white man aged 48, presents a 4 to 6 inch (10 to 15 cm.) granulomatous, fungating, ulcerated, indurated, raised lesion with rolled border on the anterolateral aspect of the right elbow. There is recent limitation of motion of the elbow. The right elbow was injured in an automobile accident eleven months ago (a bruise in an old scar of lupus vulgaris). Within two weeks a pea-sized hyperpigmented papular lesion developed. This rapidly increased to its present dimensions. In 1919 Dr. Hartzell diagnosed a lesion on the patient's right elbow as lupus vulgaris. This lesion regressed under roentgen ray therapy, with the formation of a scar. There is no history of the ingestion of drugs. The patient's father and mother died of tuberculosis. The Wassermann reaction of the blood was negative. A roentgenogram of the region of the right elbow (osseous components) at another institution was normal. A roentgenogram of the chest showed no evidence of tuberculosis. Dr. Weidman reported a histologic diagnosis of squamous cell carcinoma. The patient received ultraviolet irradiation for ten days prior to admission to the hospital.

NOTE.—Study of two additional biopsy specimens failed to substantiate the original histologic diagnosis of carcinoma. The lungs were normal on roentgen ray examination with the exception of an old, apparently healed area of tuberculosis in the apex of one. The bones of the elbow showed atrophy from disuse and some shadows which could not be interpreted definitely as an advance of the cutaneous lesion.

Multiple Hemangioma (Presented for Discussion as to Further Treatment). Presented by DR. HAROLD M. JOHNSON (by invitation).

V. F., a white man aged 26, first noticed small erythematous papules on the side of the neck at the age of 5 years. These gradually increased in number and size until five years ago and have always been asymptomatic. The patient, a well developed man, now presents many scattered hemangiomas, ranging in diameter from 3 mm. to 1 cm., on the right side of the chin, neck and preauricular and postauricular regions. There are similar lesions on the left side of the forehead. At this site there is also a linear hemangioma. There is also a verrucous nevus on the bridge of the nose. The general physical and neurologic examinations gave negative results. The Wassermann reaction of the blood was negative. A roentgenogram of the skull is normal. Histologic examination of one of the lesions showed diffuse vascular dilatation in the corium. There was a small projection above the general epidermal surface which was composed of dilated vessels. The patient has been given injections of sodium morrhuate and applications of solid carbon dioxide to the lesions of the nose and neck. Electrodesiccation was tried on small papules on the neck, and Chaoul therapy (moderate) to the lesions of the forehead in doses of 4 to 300 r (1,200 r total) was applied. The result so far has been unsatisfactory.

DISCUSSION

DR THOMAS BUTTERWORTH, Reading, Pa It is generally well recognized that in many cases of vascular nevi involving the trigeminal area the condition is associated with hemangiomas occurring in the brain and mental deficiency, neurologists call the condition nevoid amentia Some years ago I had a patient (report unpublished) with a large hemangioma involving the lower lip Roentgen ray studies revealed a calcified hemangioma of the skull Colloidal thorium dioxide (thorotrast) was injected into the internal carotid artery, producing good visualization of the larger vessels on the surface of the brain and around the optic chiasm, but the nevus was no better visualized than on the flat roentgenogram One can demonstrate angioma within the brain only when there is calcification Not all such nevi become calcified

DR J V KLAUDER I think that in some of the cases to which Dr Butterworth has made reference the eyegrounds have shown vascular changes This further emphasizes the importance of correlating lesions on the skin with changes in the eyeground

Intraepidermal Epithelioma Presented by DR JOHN W LENTZ (by invitation)

F L A, a white man aged 69, presents a superficial pigmented plaque on the abdomen near McBuney's point There is no telangiectasia, scaling or inflammatory reaction The lesion has been present for four years and is at the site pinched by a supportive belt It began as a minute brown macule There is no history of ingestion of drugs The Wassermann reaction of the blood was negative Histologic examination showed superficial basal cell epithelioma

DISCUSSION

DR SIGMUND S GREENBAUM I am particularly interested in intraepidermal epithelioma because the pathologists do not always call these lesions epitheliomas Dermatologists, I think, readily recognize the lesion as superficial epithelioma, but the infiltration is so fine and so superficial that it becomes visible only on stretching the skin

A Case for Diagnosis (Herxheimer Reaction? Gumma? Nonspecific Infected Granuloma?) Presented by DR HAROLD M JOHNSON (by invitation) for DR JOSEPH STOKES

M B, a thin, pale 12 year old boy with destruction of the entire upper lip, the nasolabial folds and the skin and cartilages of the nose, was well until Sept 1 1937, when his right lacrimal sac became infected Each side of the nasal cavity now presents excessive granulation tissue, which is covered with purulent exudate The front teeth are loosely held by the soft gum tissue There is beginning entropion of the inner canthus of the right eye The hard palate and the larynx are normal He was given seventeen high voltage roentgen ray treatments by a radiologist Shortly afterward the nasal bones began to be eroded, and small pieces fell out during nasal irrigation A positive serologic reaction of the blood was obtained, and the patient was treated with neoarsphenamine (0.45 Gm), iodides and mercury After continuous therapy with twenty-five injections, the tissue response was excellent, but the nasal discharge remained He was then given a bismuth compound intramuscularly and mercury inunctions, with no improvement in the discharge Arsenical treatment was resumed, but a severe local flare-up of the inflammation of the cartilaginous structures in and about the nose occurred The arsenical was increased to semiweekly treatments, but the tremendous destruction continued In about December 1939 he came to the pediatric department Treatment with zinc peroxide packs, saline solution and potassium permanganate irrigations was ineffectual Allantoin and cod liver oil ointment gave decided improvement Antisyphilitic therapy was resumed with small doses of bismuth

salicylate preparatory to bismarsen (bismuth arsphenamine sulfonate). The patient has made such rapid improvement during the last two months that a skin graft and plastic repair of the nose and lip are being made. The family history and laboratory studies are not significant as far as syphilis and other pertinent data are concerned. Histologic study showed a foreign body type of reaction. A roentgenogram of the chest was normal. A tuberculin test with old tuberculin gave a negative reaction. A complete blood count was within normal limits. The Wassermann reaction of the blood was positive. The cerebrospinal fluid showed medium positive serologic reactions; the other tests gave normal results. Roentgenograms of the face showed destruction of the bones. The result of a guinea pig inoculation of material from the tissue was negative. The treatment consisted of zinc peroxide packs, potassium permanganate and saline solution irrigations, ten injections of bismuth subsalicylate, seven injections of bismarsen and the local application of azochloramid in olive oil.

DISCUSSION

DR. J. V. KLAUDER: If arsenic was given prior to the roentgen ray therapy, it recalls the idea of the undesirability of giving roentgen ray treatments to persons who are receiving arsphenamine, in view of the exaggerated reaction that is alleged to result from the roentgen rays.

DR. JOHN H. STOKES: It seems to me that the boy has pursued so erratic a course, from the standpoint of conventional ideas of treatment, that one has to be careful about saying that what occurred after something else was due to what preceded it. From the start we guessed wrong on what was the appropriate treatment for this lad. His first startling improvement occurred under pediatric management with cod liver oil locally. For subsequent measures we advised fever therapy, but our advice was not taken, and I must say the improvement gained under the milder management was striking and interesting. The possibility that there is an infection we have not recognized, an allergic response to infection or a flare-up of an intercurrent infection deserves as much consideration as the relation of the arsenical treatment to roentgen ray therapy.

DR. HERMAN BEERMAN: Dr. Richmond Holcomb (retired), of the navy, saw this boy after Dr. Stokes did, and he thought the condition was syphilis of the center of the face. He has encountered about 900 cases of this type in Guam. He did not think the appearance had anything to do with the treatment or anything else but the disease itself. He has also encountered several similar cases in Philadelphia.

DR. JOHN H. STOKES: Some of these processes in the center of the face do not have anything to do with syphilis, although one may connect the syphilis with the condition in some remote and devious manner or even directly.

DR. J. V. KLAUDER: I think Dr. Holcomb is of the opinion that gangosa is also due to syphilis.

DR. SIGMUND S. GREENBAUM: I think that the etiologic diagnosis here depends entirely on the result of the serologic test. There is a condition, a granuloma of the lip, described abroad as lupus pernio mutilans, which is characterized by the progressive destruction of the center of the face and of the palate.

A Case for Diagnosis (Nonspecific Chronic Granuloma? Hypertrophic Lichen Planus? Lichenificatio Gigantea?). Presented by DR. JOHN W. LENTZ (by invitation).

U. C., a white man aged 63, of normal appearance for his age, presents: (1) a lichenified hyperpigmented plaque on the anterolateral aspect of the left leg, (2) a palm-sized, erythematous, elevated hyperpigmented plaque in the left groin, (3) rhinophyma and (4) chronic interdigital dermatophytosis of both feet. The condition had its onset thirteen months ago on the anterolateral aspect of

the left leg and in the left groin as erythematous plaques with nocturnal pruritus. Scrapings and cultures were negative for fungi. Examination of the urine for sugar, bromides and iodides gave negative results. The dextrose tolerance test gave a normal curve. The Wassermann reaction of the blood was negative. Psychiatric study revealed no abnormalities. On Nov 22, 1939 histologic examination showed vegetative dermatitis and hypertrophic lichen planus. After treatment, on Jan 18, 1940 the histologic picture was the same. On February 7 the histologic picture suggested a questionable nonspecific chronic granuloma, but hypertrophic lichen planus could not be eliminated. Treatment with strong keratolytics produced no regression of the lesion and but slight reduction of the pruritus. Roentgen ray therapy (1,300 r, with a 1 mm aluminum screen) produced slight results on both itching and lesions. The application of solid carbon dioxide produced both regression of the lesion and reduction of the pruritus.

DISCUSSION

DR SIGMUND S GREENBAUM. One should not make a diagnosis of hypertrophic lichen planus without making an examination for local amyloid disease. Such an examination is especially desirable in this case, because the lesion on the lower third of the outer surface of the left leg is suggestive indeed.

Streptococcic Infection of the Ears Presented by DR NORMAN R INGRAHAM (by invitation)

A K K., a white woman aged 27, has had recurrent episodes of small furuncles and discrete follicular, pustular lesions of the body and extremities for the past seven years. There has been inconstant and recurrent discharge from the left ear for many years. When first seen by us, on April 24, 1930, she had infectious eczematoid dermatitis of the left auricle. Recurrence of the aural condition followed temporary improvement after a variety of procedures, including mastoidectomy, administration of sulfanilamide internally and locally, roentgen ray treatment, application of ammoniated mercury ointment, 3 per cent ichthammol ointment, potassium permanganate compresses, staphylococcus toxoid, sulfur and salicylate acid ointment, phenylmercuric nitrate (1:1,500), hydrous wool fat and aquaphor (an oxycholesterol-petrolatum ointment base) and alcohol compresses, insufflation of Sulzberger's iodine powder, a low carbohydrate and allergen-free diet and shampoos. The process has shown a flare-up at the menstrual period and exacerbations under worry and mental stress. Roentgenograms of the mastoids on March 26, 1940 showed that the cells of both mastoid regions were considerably increased in density and that on both sides there were many remaining areas which could be pneumatic cells or could be small abscesses. Cultures of material from the cutaneous surface of the canal and auricle of the left ear (March 10, 1939) yielded hemolytic *Staphylococcus aureus* and hemolytic *Streptococcus anginosus*. On March 22, 1940 cultures of material from the canal of the ear contained hemolytic streptococci, hemolytic staphylococci and diphtheroids. A culture of the material from the throat showed rare hemolytic streptococci, many nonhemolytic streptococci, *Streptococcus viridans* and *Haemophilus influenzae*. Controlled intracutaneous tests with hemolytic staphylococci and staphylococcus ambotoxoid gave positive results in twenty-four hours. Repeated blood counts have been normal. The values for blood sugar and the results of dextrose tolerance tests were normal. Complete allergy studies gave no leads. The patient is presented for therapeutic suggestions.

Streptococcic Cellulitis of Elephantiasis Nostras Type (Recurrent) Presented by DR DONALD M PILLSBURY and DR CLARENCE LIVINGOOD (by invitation)

A C., a white woman aged 41, apparently in good health, presents a dusky erythema of the skin anteriorly and inferiorly and along the sides of the nose,

together with a rather brawny edema of the same sites. The local picture changes considerably from time to time. The condition had a sudden onset with headache, chills and fever accompanied by edema and erythema of the face in January 1939. It subsided, leaving a residual erythema. There was a similar attack in March and in July and to a lesser extent each month since then, each time two to three days before her menstrual period. She has had measles, mumps, scarlet fever, pneumonia, frequent colds and chronic sinusitis, and a "nervous breakdown" occurred five years ago. A complete blood count showed: 75 per cent hemoglobin and 3,810,000 erythrocytes and 5,950 leukocytes per cubic millimeter, with 72 per cent polymorphonuclear leukocytes, 23 per cent lymphocytes, 4 per cent monocytes and 1 per cent eosinophils. Serologic tests for syphilis gave negative reactions.

DISCUSSION

DR. J. V. KLAUDER: I think the administration of sterile milk intramuscularly will help both of these patients. For the first patient I would suggest mercuriophen, 1 grain (0.06 Gm.) to a 6 ounce (170 cc.) mixture, as a lotion.

DR. THOMAS BUTTERWORTH, Reading, Pa.: I think patients with a condition like this do better with liquids and lotions than with greases.

DR. LOUIS GOLDSTEIN: For patients with periauricular dermatitis I have used gentian violet. After the vesiculation and excoriation have cleared and the inflammation has subsided, I use roentgen rays. This therapy has given me good results.

DR. MORRIS MARKOWITZ: I think that ointment of coal tar is one of the best applications for these conditions.

DR. JOHN H. STOKES: Alternations of 10 per cent ammoniated mercury ointment with ointment of coal tar yield satisfactory results, but the dermatosis relapses. At least, I have not been able to maintain the good result.

DR. SIGMUND S. GREENBAUM: Some years ago I had occasion to use streptococcus toxin for a patient with erysipelas, and I think subsequently in 2 other patients I was able to produce immunization to the point where repeated attacks were prevented. Only yesterday one of these patients told me that she had not had an attack of erysipelas for eight or nine years. I am wondering whether an attempt should not be made to obtain the streptococcus that may be the cause of this condition and an attempt made at immunization with its filtrate.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: Has any one used antiviral ointments for these conditions? They are ointments made up from the filtrates of streptococci and staphylococci.

Congenital Linear Pigmentation of Negroes. Presented by Dr. HAROLD M. JOHNSON (by invitation) and Dr. DONALD M. PILLSBURY.

H. G., a Negro aged 49, has noted a linear pigmentation on the lateral side of the arms since childhood. No other similar pigmentation was noted elsewhere on physical examination. Routine examination of 200 Negroes revealed this pigimentary line in 31.5 per cent of them. Ten per cent of the patients showed such lines on both arms. The pigmentation was sharply demarcated, extending from the tip of the acromial process along the border of the arms and fading into the cubital fossa. Histologic examination showed normal epidermis with increased pigmentation. There was slight acanthosis with increased pigmentation at one end of the epidermis, probably designating the line of demarcation.

DISCUSSION

DR. J. M. SCHILDKRAUT, Trenton, N. J.: To me that line looked lighter than the rest of the skin.

DR. HAROLD M. JOHNSON (by invitation): Dr. Pillsbury and I have been interested in this linear pigmentation. In the literature the only thing I could find was a short article (Futcher, P. H.: *Science* 88:570 [Dec. 16] 1938) in which the

line was not considered congenital. According to Fitcher, the histologic examination showed nothing abnormal. We believe that in 10 per cent or more of our cases the condition is probably congenital. I have written to the professors of embryology at Tulane University, at the University of Nebraska and at Johns Hopkins University and talked to professors of embryology at the University of Pennsylvania. No one could give me information on this anthropologic problem.

Diffuse Morpheiform Type of Scleroderma with Calcinosis (Thibierge-Weissenbach Syndrome) Improvement under Prostigmine Bromide Therapy Presented by DR C C THOMAS

M. L., a thin, gaunt, white woman aged 24, presents slight stiffening of the skin about the mouth and chin. There are the remains of a former sclerodermatous band extending to the wrist on the inner aspect of the forearm and the dorsum of the right hand. There is also a slight residual brownish pigment in these regions. There is now about 50 degrees of motion in the right wrist joint. Large deposits of calcium can be felt over both anterior iliac spines. A small deposit is palpable on the ulnar aspect of the right elbow joint and on the right knee. There are contracture and hardness of the hamstring muscles. The condition had its onset in the fall of 1934 with itching of the hands. Gradually the fingers became stiff. This continued during the next year, coincident with the patient's first pregnancy. During 1936 the skin of the dorsa of the hands, forearms and chest became brownish. In 1937 the skin became lardaceous and shiny, the fingers were contracted in flexion, the wrists became immobile, and the lower third of the face and the skin of the "V" of the neck became shiny, firm and hard. The mouth could hardly be opened. On the inner surface of the right arm a brownish, thickened band spread from wrist to forearm. In 1939 deposits of calcium were discovered in the heels, near the elbow joints and over the iliac spines. A stiffness of the hamstring muscles developed, and pain of the right wrist joint with absolute rigidity began in December. The patient has had varicella, measles, influenza and pertussis. In November 1937 the basal metabolic rate was +19 per cent, the serum calcium 9.1 mg, the serum phosphorus 4 mg and the blood cholesterol 102 mg per hundred cubic centimeters. In January 1940 the calcium amounted to 9.6 mg and the phosphorus to 4.2 mg per hundred cubic centimeters of serum. The blood count was normal except for 7 to 10 per cent monocytes and 4 per cent eosinophils. Results of other studies were normal. Roentgenograms of the elbows, feet and pelvis showed deposits of calcium. Between 1937 and January 1940 two hundred and twelve treatments of acetylbetamethylcholine (methyl) iontophoresis resulted in considerable improvement. The patient's condition remained stationary, however, during 1939. Since Feb. 20, 1940 the patient has had oral medication with prostigmine bromide, 0.015 Gm, nine tablets daily, with decided improvement, resulting in loss of pain and return of motion to the right wrist, softening and decrease in the size of the morpheiform patches and increase in strength and motility of the hands.

DISCUSSION

DR C C THOMAS. The first reason for presentation of this woman is that the appearance of the calcinosis coincided with improvement of the scleroderma. This is interesting because increased tissue calcium has been reported in scleroderma, and it is probable that it was precipitated out in the form of calcium deposits and coincident with clinical improvement. Secondly, for about a year the patient's condition had been stationary, but in the last two months she has improved markedly under the administration of prostigmine, a bromide which, to my knowledge, has not been tried previously in scleroderma. I think it is a promising form of treatment.

DR J M SCHILDKRAUT, Trenton, N. J. I showed a man about a year ago with diffuse scleroderma. His skin cleared up with the administration of pancreatic extract.

Chronic Pyogenic Dermatitis of the Hands and Feet with "Bacterid" on the Arms and Trunk. Presented by DR. DONALD M. PILLSBURY and DR. CLARENCE LIVINGOOD (by invitation).

M. F., a white man aged 24, healthy looking, alert and cooperative, has an erythematous crusted plaque on the dorsum of each hand and on the outer surface of the right ankle. The flexor surface of the entire right arm and the upper part of the left arm is the site of an erythematous, oozing and superficially crusted dermatitis, with individual similar lesions on the back and inner surfaces of the thighs and a few receding lesions on the face (a hematogenous distribution). The family history shows no pyogenic tendencies in any of the members; the father of the patient is allergic to sea food. The patient had a series of furuncles at the age of 8 years, at 15 and at 16. He had a mastoidectomy at the age of 12 years. He had cellulitis of the hands at the age of 13. The blood serologic tests for syphilis were negative. The complete blood count was within normal limits except for 8 per cent eosinophils. The urine was normal. The lesion gave a pure culture of hemolytic *Staphylococcus aureus*. Three and a half years ago the patient had a vesicular eruption on the outer surface of the right ankle, with a similar eruption on the dorsum of both hands about two weeks later. It has persisted to date without complete clearing at any time, although he has had many periods of temporary improvement following roentgen ray treatments, particularly two weeks ago. One week after an intradermal injection of staphylococcus toxoid (1:100) by another physician, he had a sudden attack of vesicular and pustular lesions on the arms, back, inner surfaces of thighs and face, with particular localization at the sites of the injection. Since then there has been coalescence of the lesions, itching and oozing, with slow improvement in the past few days. The patient has had many different types of local treatment since the onset of the generalized eruption, consisting of potassium permanganate baths, mild antiseptic ointments, sedatives, dilute hydrochloric acid, calcium gluconate and histaminase. An injection of autogenous whole blood caused a moderate chill, which responded quickly to an injection of epinephrine.

DISCUSSION

DR. SIGMUND S. GREENBAUM: On what basis was the diagnosis of generalized "staphylococoid" made?

DR. CLARENCE LIVINGOOD (by invitation): Because the eruption on the body occurred after the injection of staphylococcus toxoid. I admit that it is a loose diagnosis.

DR. SIGMUND S. GREENBAUM: I think it is a good diagnosis, but on the hand the man has a vesicular eruption. I have given many injectins of staphylococcus filtrate, using staphylococci of extreme virulence for making the filtrate and organisms that produced extremely strong toxins, but I have never seen a generalized eruption of this sort.

Linear Scleroderma with Facial Hemiatrophy. Presented by DR. ROBERT C. LOFGREN (by invitation).

Mrs. A. B. C., a white woman aged 26, in apparent good health, gave a history of injury to the right side of the body. Fifteen years ago white spots developed on the front of the right thigh. They gradually spread down her right leg and up the right side of her body to the thorax. There were no associated symptoms during this time. Erysipelas developed on the right leg about six months after onset of the present trouble. She improved with massage, heat, exercise and ingestion of thyroid. About 1936, shortly after the birth of her only child, she noticed that her right leg was getting smaller than the left. This has progressed to the present. There has been no diminished strength, coldness or numbness of the affected limb. She has complained of occasional stiffness and pain in the right knee during the winter. Occasionally serum discharges from a sinus on the

anterior part of the right thigh. Examination revealed scattered plaques of atrophic skin. One of these, about 3 inches (7.5 cm) in diameter, is located on the left upper part of the back. There is also a linear lesion on the right side of the back, which begins near the spine and extends around the thorax to the right breast, to the groin and down the thigh over the knee to the inner malleolus of the ankle. There is another lesion over the left iliac region. These plaques are slightly depressed, and blood vessels are clearly visible through the thinned epidermis. The right leg is smaller than the left, averaging about 4 to 6 cm less in circumference at the ankle, calf, knee and thigh. Her forehead appears slightly asymmetric and depressed on the right side of the midline. There is an area of alopecia of the scalp about 4 cm in diameter. The neurologic examination showed no abnormality. The Wassermann reaction of the blood was negative. Examination of the blood showed 10.2 mg of calcium and 3.5 mg of phosphorus per hundred cubic centimeters. Roentgenograms of the skull, thorax, vertebrae and legs revealed only slight demineralization of the right lower extremity. The basal metabolic rate was +12 per cent in 1926. The patient was treated with thyroid extract, solution of potassium arsenite U. S. P., pituitary extract, ultraviolet irradiation, exercise and massage on her first admission (1926 to 1929), with definite improvement. Since the last admission she has received bismuth hydroxide and massage.

DISCUSSION

DR JOHN H. STOKES: I do not think that there is facial hemiatrophy here. There is a depression in the skin to the right of the midline, extending from the forehead into the hair, but there is no asymmetry when one looks at the nares and the contour of the nose from below. What I imagine has occurred is that the woman has had a plaque of morphea in her scalp, and the atrophic residue is now seen in the skin, rather than a true facial hemiatrophy. I asked the patient about the date of the injury and she said she was 10 years of age when she fell off a porch roof. I suspect that the morphea developed after she had reached adult growth. There are none of the usual accompaniments of hemiatrophy in this case. There is no recession of the eyeball, the nares are practically identical in flare and shape, and the upper lip is bilaterally symmetric.

DR ROBERT C. LOFGREN (by invitation): As far as the patient can remember, the lesion of the scalp occurred simultaneously with the scleroderma, when she was 12 years old.

DR JOHN H. STOKES: That is an age at which hemiatrophy should have developed, she may have a partial hemiatrophy. The roentgenograms show the skull to be symmetric, so I do not see how that can be called hemiatrophy.

DR ROBERT C. LOFGREN (by invitation): The roentgenograms showed slight demineralization of the right leg as compared with the left. My own impression is that there is atrophy of the subcutaneous tissue due to scleroderma. The patient says there is apparently no diminution in the strength of the leg, it is as good as the other and her job requires constant standing. She walks evenly.

Two Cases of Ehlers-Danlos Syndrome Presented by DR JOHN A. FRITCHEY (by invitation), Harrisburg, Pa., and DR SIGMUND S. GREENBAUM

B. C. M., a white man aged 43, presents atrophic scars, containing one pseudotumor in the scar of the left knee, on the shins, forearms and forehead (frontal bosses). The integument in the scar is loose, slightly wrinkled and slightly depigmented and contains no appendages (hair or glands). The skin over the entire body, especially over the bony prominences, is hyperelastic, with no change in the appendages of the skin. The joints of all of his fingers are hyperflexible, but no laxity is noted in the larger joints. No lesions are present on the mucous membrane, but the lips show hyperelasticity as part of the general picture. The sides and back of the scalp and the left ear show greasy scaling areas on an erythematous base.

S. M., a white girl aged 13 (daughter of the preceding patient), presents atrophic, slightly hyperemic scars containing no tumor masses on the shins, fore-

arms and forehead. There is a tendency to keloidal formation, as seen over the right shin. The skin of the entire body is hyperelastic, with no change in the appendages of the skin other than keratosis pilaris involving especially the arms and thighs. No lesions are present on the mucous membrane, but hyperelasticity of the lips is noted. The father noticed that her skin had a tendency toward fragility since infancy and has tried to protect her as much as possible from injury, but in spite of all care some injuries have occurred, especially on the shins, the forearms and the forehead, resulting in scars. Hyperlaxity of the small joints and hyperelasticity of the skin have been present from infancy. The father states that from time to time he has noted small tumor masses in the scarred areas.

DISCUSSION

DR. JOHN H. STOKES: This is the sort of condition which twenty years ago was spoken of as the localized form of epidermolysis bullosa and also frequently as dystrophia bullosa congenita of Werther and Noble. The original illustration appeared in one of the old numbers of the original Neisser *Ikonographia*. This dermatosis is not uncommon and is usually accompanied by a certain degree of cutis elastica. It generally turns up when a patient starts to play football, and then it is clearly recognized that his shins are different from the shins of other players. He gets lesions just over the kneecap, and the skin of the arm can be stretched 6 inches (15 cm.) with no strain on the skin.

DR. JOHN A. FRITCHEY (by invitation), Harrisburg, Pa.: The father has one of those pseudotumors today. I noticed it in the scar on his left knee. He says his daughter occasionally gets them; they come and go.

DR. SIGMUND S. GREENBAUM: The father called my attention to his elastic skin when he consulted me for another condition. At first I thought it was epidermolysis bullosa, but there is no history of bullae. Also, trauma did not produce bullous lesions, but the skin would break, with atrophic areas of healing following. The only other member of the family affected was his daughter; she had practically all the phenomena he had, but not so extensively.

DR. THOMAS BUTTERWORTH, Reading, Pa.: Another point to be brought out in this matter of differentiation between epidermolysis bullosa and Danlos' syndrome is that in inheritance the Danlos syndrome is a dominant characteristic, while the dystrophic form of epidermolysis bullosa is recessive. This is evidently a dominant characteristic, which would be in favor of the condition being Danlos' syndrome.

JOSEPH V. KLAUDER, M.D., *Chairman*

HERMAN BEERMAN, M.D., *Secretary*

May 17, 1940

Localized Alopecia of the Eyebrows and Lashes (Alopecia Areata? Trichotillomania?). Presented by DR. E. R. GROSS, Wilmington, Del.

E. L., a white boy aged 14, well developed and apparently in good health, shows scanty lashes on both lower lids and none on the upper lids. The eyebrows present a stubby growth of sparse hair. The process began in September 1939, and three days after onset there was total alopecia of the lashes and eyebrows. The patient has always been nervous.

DISCUSSION

DR. REUBEN FRIEDMAN: I suggest trichotillomania. The clinical appearance is not that of alopecia areata. The patient's father told me that the boy is nervous

and creates scenes at home. In addition, there is a history of domestic discord. The father was recently discharged from a hospital, where he was confined for two weeks for a "nervous breakdown." The mother has left the family on four different occasions to go off with another man. The boy, who is an only child, is in constant conflict with the mother on one side and the father on the other. The father also told me that he has repeatedly noticed his son plucking hairs from his eyebrows and eyelashes.

DR FRED D WEIDMAN. I had the same impression when I first looked at the patient, but I did not go into the history in detail. In this condition the hairs need not necessarily be plucked out. They may be largely rubbed out. Incidentally, there have been epidemics of this artificial alopecia of the eyebrows in penal and other institutions. One person gets the habit of rubbing out his eyebrows, and it is taken up by the other inmates. Such endemic alopecia was at first considered evidence in favor of the infectious origin of alopecia areata until the true cause was disclosed.

DR JOSEPH V KLAUDER. So-called epidemics of trichotillomania of which Dr Weidman speaks are probably the result of suggestion and mimicry, which also play important roles in the use of cosmetics and tattooing and in human adornment. I have discussed this elsewhere in more detail (*Psychogenic Aspects of Skin Diseases, J Nerv & Ment Dis* 84: 249-273, 1936).

A Case for Diagnosis (Leprosy? Rheumatic Nodules? Circumscribed Myxedema?) Presented by DR EVAN B HUME (by invitation) for DR EDWARD F CORSON

Y D, a slightly built Chinese man aged 40, with a pitted face and protruding eyes and carrying his head slightly tilted back, presents on the extensor surfaces of the lower half of the legs several nodules which are discrete, spherical and hard and are not attached to underlying structures. They vary in size from 0.5 to 1.5 cm in diameter. There is no redness, tenderness or pain, and sensation is not so acute over the nodules as on the surrounding skin. The lateral third of each eyebrow lacks hair. There is patchy loss of hair of the scalp. The forehead appears to have thickened skin, but no nodules are noted. The skin over the right first carpometacarpal joint is red, swollen and hot, owing to inflammation of the joint. The ulnar nerves at the elbows are doubtfully thickened. Medical examination revealed paralysis of both superior rectus, both external rectus and both inferior oblique muscles. Exophthalmometer readings were right eye, 15, left eye, 17-18. Visual acuity was 20/30 and 20/30, and the visual fields were normal. The nasal septum was thickened, and he had a chronic right frontal and bilateral maxillary sinusitis. The patient was born in China and came to the United States twenty years ago. He suffered a severe attack of smallpox at the age of 8 or 9 years but stated that he had had no other diseases. Roentgenograms of the chest show increase in the root shadows and peribronchial markings but no evidence of tuberculosis. On Feb 2, 1940 he came to the neurologic department, where he was found to have blurring of the left optic disk, diplopia and impaired vibratory sense in the feet to just above the ankles. On February 14 a roentgenogram of the skull showed no evidence of increased pressure, but the anterior and posterior clinoid processes of the sella turcica were suggestive of localized pathologic change, probably a suprasellar space-taking lesion, and there were some indistinct areas of density just above the dorsum. The Wassermann and Kahn reactions of the blood were negative on several occasions. Wassermann reactions of the spinal fluid were negative, and gold curves were normal. The blood count and the urine were normal. Two scrapings from the nasal mucosa, made two weeks apart (the second after the administration of potassium iodide orally), contained no lepra bacilli. The basal metabolic rate was repeatedly normal. A biopsy specimen obtained in a New York hospital on Oct 23, 1939 showed "Circumscribed edema, myxomatous in type, in the deeper fibrous portion of the skin, without proliferation and appearing to be a degenerative process. Practically no infiltration."

DISCUSSION

DR. DONALD M. PILLSBURY: If I understand correctly, there has been no absolute evidence of leprosy in this case. The patient has definite bilateral exophthalmos and is thin, but he has no other evidence of hypothyroidism. Because of the exophthalmos and because these nodules are principally over the pretibial region, I should like to suggest a diagnosis of circumscribed myxedema. The lesions are apparently not characteristic of the ordinary plaque type of localized myxedema in which one has, as a rule, one or two fairly large plaques with a pigskin appearance of the overlying skin. In this case there are about four or five nodules, and the skin over them appears normal. It would be possible for this patient to have circumscribed myxedema without frank hypothyroidism now, since the lesions may persist after the toxic reaction has subsided.

DR. FRED D. WEIDMAN: I do not think this condition is leprosy. These nodules are wooden. I surmise that they are of the order of dermatofibroma lenticulare or, if not quite that, that they conform somewhat with multiple subcutaneous xanthoma, which Broders has described (Broders, A. C.: *Benign Xanthic Extraperiosteal Tumor of the Extremities Containing Foreign Body Giant Cells*, in *Collected Papers of the Mayo Clinic, Philadelphia, W. B. Saunders Company, 1919, vol. 11, p. 1302*). I should like to see histologic sections. I believe that the lesions are not those of a fundamental disturbance of lipid metabolism—that is, not one of the cutaneous lipoidoses—but are fibromatous changes which usually come about through traumatism. In some fibromas xanthoma develops in the cells as a secondary change. I think for practical purposes that the lesions in this case are subcutaneous fibromas. I noted in the history that there was a lesions above the pituitary. This finding would throw more light on the xanthoma question. The pituitary is a location where xanthomas can develop, as in Christian-Schüller disease, for example.

Multiple Pigmented Nevi (Malignant?). Presented by DR. DOUGLASS A. DECKER, Allentown, Pa.

Mrs. C. A., a white woman aged 25, presents two hundred and thirty-seven pigmented lesions scattered over the entire body. On the left shoulder there is a 2 cm.-sized, deeply pigmented, nonhairy plaque that has developed in the past nine months. On the right cheek there is a bean-sized, jet black, nonhairy nodule that has developed also in the past nine months. The patient has had many "moles" all her life. A nevus was removed from her left arm three years ago and another from the left breast a year ago. In the past nine months the number of lesions has doubled, and the lesions on the left arm and on the right cheek have grown to their present size. One pathologist stated that the histologic sections showed evidence of malignancy, while the second states that there are no such signs. The patient has received no treatment.

DISCUSSION

DR. FRED D. WEIDMAN: I do not think that these lesions are malignant now. I think the lesion on which biopsy was performed could be regarded as a "malignant freckle." There is so much sooty black mixed in with the brown that I should say it bodes ill at some future time. Dr. Decker was particularly concerned with the rapid development of additional lesions. In the past three months something like a hundred new lesions have developed. In spite of that fact, I do not think they are metastatic lesions. I think they represent a delayed development. In benign nevi, particularly those at the dermoepidermal junction, cells with remarkably large and deceptive nuclei are observed. One cannot regard these large cells as malignant unless there are other associated features of malignancy.

DR. ROBERT L. GILMAN: I think these cases are extremely important from the patient's and from the physician's standpoint, since physicians frequently have to decide clinically whether a condition is malignant or not. It is becoming a

problem to reassure the patient that what he has is merely an outcropping of delayed-appearing nevi rather than a metastatic condition

DR DONALD M PILLSBURY Has there been anything in this woman's general medical background to explain to some extent the rapid increase in the number of lesions?

DR JOSEPH V KLAUDER I do not believe that the lesions are malignant I agree with Dr Weidman, although the patient presents two of the signs of malignancy

DR ROBERT L GILMAN One of my patients with similar lesions noticed an increase in superfluous hair Although there has been no study of the adrenal glands, I was informed that for five weeks prior to the appearance of these lesions this patient had been taking large doses of thyroid

A Case for Diagnosis (Granuloma Annulare? Annular Erythema Multiforme Perstans? Erythema Elevatum Diutinum? Intraepidermal Epitheliomatosis? Porokeratosis of Mibelli?) Presented by DR H A SAMITZ (by invitation)

L O, a white woman aged 46, presents lesions restricted to the dorsal aspects of the hands, with two larger lesions on the right hand and four smaller ones on the left The lesions are all of the same character but vary in size from 0.5 to 5 cm in diameter They are distinctly annular, with pinkish raised borders consisting of coalesced papules The centers of some lesions appear slightly atrophic There is no induration or scaling In the past months discrete papules have appeared on the forearm The eruption on the hands is of four years' duration There are no subjective symptoms referable to the dermatosis The patient has hypertensive cardiovascular disease and is passing through the menopause The urine and a complete blood count were normal The basal metabolic rate was +8 per cent The serologic reactions of the blood were negative On Jan 13, 1940 Dr Weidman made a histologic diagnosis of foreign body granuloma (on the basis of degenerate collagenous and elastic tissue and foreign body giant cells) On February 10 another section suggested acrochordon (hyperplasia of the epidermis and degeneration of fibrous tissue) The patient was given four roentgen ray treatments, with negligible results

DISCUSSION

DR FRED D WEIDMAN The extreme atrophy of the center of that lesion is something that is not seen in regressing granuloma annulare If this lesion were to regress, there could be no restoration of the central parts to normal There is no question that the lesion is a granuloma, in view of the infiltrated margins I have encountered several cases like this in which the diagnosis of porokeratosis of Mibelli has been suggested Dr Wright has often criticized this diagnosis There are two types of porokeratosis of Mibelli one, the classic type with the furrowed margin, and the other this type Histologically, the infiltrated margins in the present case show the picture of a foreign body granulomatous reaction (Schnabl, E A Case of Porokeratosis Mibelli, *Arch f Dermat u Syph* 157 207, 1929) It seems that four years is a long time for granuloma annulare to persist

DR HERBERT J SMITH Several months ago the lesion looked like a typical granuloma annulare Tonight the picture has changed, since at that time the edges were distinctly raised and there was not the decided atrophy of the center that is present now

DR MORRIS MARKOWITZ Two years ago I presented a case of this condition on the dorsum of the hand in which Dr Weidman made a diagnosis with the same results as now Dr Greenbaum at that time said that the condition was intraepidermal epithelioma

DR. CARROLL S. WRIGHT: I examined this patient carefully with porokeratosis of Mibelli in mind. One should not always try to make that diagnosis only on lesions with the exact textbook description. This patient's eruption does not fit in with true porokeratosis of the type I described in 1921 (ARCH. DERMAT. & SYPH. 4:469 [Oct.] 1921). In my case all the lesions had a little furrow running around the top of the ridge. There is a central atrophy in porokeratosis, and when one makes a cross section in this ridge there is a little overlapping, like an awning, coming over on one side. In the microscopic sections one sees many dilated follicles with large plugs in them. Matsumoto (*J. Cutan. Dis.* 34:489, 1916) in Japan described an unusual case of porokeratosis and declared that all examples of this disease do not look alike. Perhaps when I argued with Dr. Weidman in the past, I tried to fit all the eruptions to the description of the lesions I studied.

Symmetric Callosities of the Toes and Soles. Presented by DR. JOSEPH V. KLAUDER.

R. K., a white girl aged 17, presents a condition which first appeared when she was 2 years old. There are pronounced callosities involving the heels and their lateral aspects and the lateral and flexor surfaces of the toes, with a few discoid callosities on the sole. The surfaces of the callosities are smooth, elevated, thickened and nonulcerative. The uninvolved skin of the sole is normal except for hyperhidrosis, which also affects the palms. The palms otherwise are normal. There is no other cutaneous involvement. There is no family history of similar involvement.

DISCUSSION

DR. JOSEPH V. KLAUDER: This patient may represent the early stage of that condition for which Kienböck suggested the term "trophopathia pedis myelodysplastica" (Kienböck, R.: Ueber Fusserkrankung bei versteckter Rückenmarksmissbildung [Trophopathia pedis myelodysplastica], *Fortschr. a. d. Geb. d. Röntgenstrahlen* 42:567-582, 1930. Foor, C. G.: Allen, E. V., and Morton, S. A.: Bilateral Trophic Ulcers and Deformity of the Feet: Report of a Case, *Proc. Staff Meet., Mayo Clin.* 6:361-364, 1931). This condition is characterized by large callosities on the soles and toes, which later ulcerate. There is a deformity of the feet, with destruction of the metatarsal and phalangeal bones associated with some evidence of congenital anomaly or disease of the vertebrae or spinal cord. This patient does not present a congenital anomaly or disease of the vertebrae or spinal cord. I have not as yet had a roentgenogram of her feet.

DR. REUBEN FRIEDMAN: Pressure and trauma may have something to do with the production of the callus in this case. The palmar aspect of the distal phalanges of the right thumb and forefinger and the subungual part of the last digit of the left thumb have begun to show the same yellowish discoloration. The patient is right handed, and it is possible that the pressure of pencil and pen in the right hand may have contributed to the formation of this callus.

DR. JOSEPH V. KLAUDER: It would be hard to explain the lesions on the sides of the toes on the basis of trauma.

DR. FRED D. WEIDMAN: Keratin is one of the substances most strongly stained by carotene. In carotenemia the yellow color is pronounced on the palms and soles. It might be interesting to inquire into the diet of the patient.

Sarcoid Type of Tuberculosis in the American Negro, with Splenomegaly. Presented by DR. CARMEN C. THOMAS.

M. M., a thin Negress aged 27, presents small miliary papules aggregated about the eyelids, and the corners of the mouth and the nose. Larger papules are present on the thorax, and another group is on the abdomen. There is generalized lymphadenopathy. The border of the liver can be felt 3 fingerbreadths below the costal border, and the spleen is tremendously enlarged, reaching almost

to the iliac crest. There are no deformities of the fingers or toes. The lesions on the face began in September 1939. In December she had acute intermittent pain in the left upper quadrant of the abdomen, which has been present off and on since then. She has had pneumonia, and she had pleurisy in 1939. A roentgenogram of the lungs made at a local tuberculosis institute on May 24 showed greatly enlarged hilar lymph nodes and scattered soft spots through the middle third of the right lung. The sputum has been repeatedly negative for tubercle bacilli. Reactions to tuberculin tests on May 24 with purified protein derivative (0.00002 mg in 0.1 cc) were 1 plus. A blood count showed 5,600 leukocytes per cubic millimeter, with an increase of monocytes. The patient has been given only symptomatic treatment.

DISCUSSION

DR FRED D WEIDMAN. There is a beautiful example of the clustering of lesions at the inner canthus of the eye, which I think is a valuable point in the differential diagnosis of this condition.

DR CARMEN C THOMAS. I have had a total of 9 cases of sarcoid disease in the Negro, and in those I was able to feel the spleen in 4 at one time or another. This woman has the largest spleen I have ever encountered in any disease.

A Case for Diagnosis (Poikiloderma? Lupus Erythematosus?) Presented by DR J M SCHILDKRAUT, Trenton, N J

H A A, a white man aged 52, presents a patchy erythematous eruption of the right side of the jaw and neck, covering an area about 7 by 4 cm. The area involved is deep red, and the skin is somewhat atrophic and telangiectatic. Follicular openings are not patent. The patient claims that the condition came on overnight about three months ago. At times there is slight itching. The condition has not changed since its inception.

DISCUSSION

DR FRED D WEIDMAN. It is rather difficult for me to come to a conclusion on such short study. I think it is agreed that there are streaks of atrophy and that between the streaks there are sometimes short ridges and at other places simple papular elevations, and I thought that some of those papules were capped with yellow. Whether that is pus or elastosis I do not know. The location and character of the papules are suggestive, at least, of ulerythema sycosiforme, and if it turns out that the caps are pustular and not simply elastic tissue, it would strengthen this diagnosis.

DR J M SCHILDKRAUT, Trenton, N J. When I saw this man, my first thought was that the eruption was lupus erythematosus. The distribution and the history that it developed overnight are rather unusual. These patches are atrophic, and there does not seem to be any adherent scale with patent follicles. There is some prominence of the follicles in places, but I think that is due to the location of the lesions in the bearded area. I think the possibility of poikiloderma should also be considered in this case.

DR JOSEPH V KLAUDER. I do not think there is sufficient atrophy to merit the diagnosis of poikiloderma or ulerythema sycosiforme. I favor a diagnosis of lupus erythematosus.

Reticuloendotheliosis Presented by DR H E TWINING

J K., a white man aged 20, was presented for diagnosis on April 22, 1938 (*ARCH DERMAT & SYPH* 38:994 [Dec] 1938), but histologically a diagnosis of reticuloendothelial tumor was made. Roentgenograms from time to time have demonstrated extensive lysis of the bone, involving the femurs, temporal bones and mandibles, with almost complete solution of the coronoid processes, the condyles and rami are also involved. The patient has been given roentgen ray therapy (75 r unfiltered, at weekly intervals), with marked improvement.

DISCUSSION

DR. H. E. TWINING: This case at present is really not a dermatologic one. Two years ago, when I presented the patient, he had lesions in the groins, around the rectum and in the canals of both ears. These lesions entirely disappeared with small doses of roentgen rays. One could almost put one's finger in the lesions in both temporal bones and in the right femur. I had to put the patient to bed for fear of fracture. With roentgen ray treatment these lesions have completely healed, but from time to time new bones become involved. Within the last two months the mandible on both sides was almost in a state of complete fracture, but with careful watching and roentgen ray treatment the boy is in good shape today. He has gained nearly 40 pounds (18 Kg.) in weight since I presented him before.

Book Reviews

Modern Dermatology and Syphilology By S William Becker, M D, and Maximilian E Obermayer, M D Price, \$12 00 Pp 847, with 461 illustrations in text and 32 full color plates Philadelphia J B Lippincott Company, 1940

Although there are numerous textbooks in English on dermatology, there is room for the new one by Becker and Obermayer because of its excellence. It is unusually well written in clear and simple language and is remarkably well illustrated. Although the book is primarily intended for general practitioners and students, it contains much valuable information for dermatologists. It lives up to its title in being modern and up-to-date. Space has been allotted to subjects according to their importance, some of the rarer dermatoses and tropical diseases of the skin having been omitted.

The authors have tried to avoid the cyclopedic type of textbook and have laid emphasis on their own ideas. Their classification of diseases of the skin differs somewhat from those commonly used. To make the volume more informal they have included a section at the beginning of each chapter which they term "orientation." As they state, this is given in the intimate language of a demonstrator to small groups of students.

An early chapter is devoted to general therapy, in which preparations recommended are arranged alphabetically. The authors have been rather generous in their mention of proprietary remedies, including cosmetic preparations, giving the names of the firms who manufacture them.

In the chapter on eruptions due to drugs, the types of eruptions produced are first tabulated, and this tabulation is followed by the list of drugs which cause various eruptions. A special chapter is devoted to allergy as it affects diseases of the skin. This difficult subject is satisfactorily discussed. An interesting chapter is devoted to occupational and industrial dermatoses. This contains a tabulated percentage of various substances with which patch tests are made (recommended by Dr Louis Schwartz).

A comprehensive discussion of the entire subject of syphilis is given in 186 pages. An elaborate chart for the treatment and control of complications is included as an insert.

The authors have followed the nomenclature of the "Standard Classified Nomenclature of Disease," with, as they say, certain revisions and additions. Why the term pompholyx is not used in place of dyshidrosis the reviewer cannot understand, especially in view of the authors' statement that the term dyshidrosis is an "obvious misnomer for a chronic recurring vesicular eruption of the hands and feet." The scholarly qualities of the authors are shown by the absence of mistakes in Latin terminology, which creep into so many American texts.

One of the most valuable features of the book is the numerous illustrations, which not only represent excellent photography but have been splendidly reproduced on glazed paper. The excellence of the black and white illustrations disproves the authors' statement that "colored illustrations are indispensable for accurate presentation of cutaneous disorders." In the reviewer's opinion, few of these illustrations would be increased in value by being colored. On the other hand, little if anything is gained by the color in the plates which depict stasis ulcer, rosacea, dermatitis factitia, pemphigus vulgaris and exudative neurodermatitis.

The bibliography at the end of each chapter is short and is intended to present most of the important publications during the past five years and the more valuable ones of previous years. The work of the publisher is all that could be desired, even though use of glazed paper throughout the book has naturally increased its weight. The book is a splendid contribution to American dermatology.

Directory of Dermatologic Societies *

INTERNATIONAL

TENTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY
Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102-2d Ave. S. W., Rochester, Minn.
Place: New York. Time: Postponed indefinitely.

PAN AMERICAN MEDICAL ASSOCIATION, SECTION OF DERMATOLOGY
AND SYPHILOLOGY
Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Austin W. Cheever, Secretary, 464 Beacon St., Boston.
Place: Buenos Aires, Argentina. Time: August 1941.

FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY
(CANADIAN BRANCH)
L. P. Ereaux, President, 1390 Sherbrooke St. W., Montreal.
F. E. Cormia, Secretary-Treasurer, 2068 Sherbrooke St. W., Montreal.

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY
H. W. Barber, President, 7 Devonshire Pl., London, W. 1, England.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1, England.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION
ON DERMATOLOGY AND SYPHILOLOGY
J. Gardner Hopkins, Chairman, 102 E. 78th St., New York.
C. F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.
Place: Cleveland. Time: June 2-6, 1941.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY
Harry R. Foerster, President, 208 E. Wisconsin Ave., Milwaukee.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.
Place: Palmer House, Chicago. Time: Dec. 8-11, 1940.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY
Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary-Treasurer, 416 Marlborough St., Boston.

AMERICAN DERMATOLOGICAL ASSOCIATION
William H. Guy, President, 500 Penn Ave., Pittsburgh.
Harry R. Foerster, Secretary, 208 E. Wisconsin Ave., Milwaukee.

SOCIETY FOR INVESTIGATIVE DERMATOLOGY
Bedford Shelmire, President, 1719 Pacific Ave., Dallas, Texas.
S. W. Becker, Secretary, University of Chicago, Department of Medicine, Chicago.
Place: Cleveland.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SECTIONAL

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

Elmore B Tauber, President, 19 W 7th St, Cincinnati
Lawrence C Goldberg, Secretary-Treasurer, 623 Doctors Bldg, Cincinnati

MISSISSIPPI VALLEY DERMATOLOGICAL SOCIETY

Elmore B Tauber, President, 19 W 7th St, Cincinnati
Lawrence C Goldberg, Secretary-Treasurer, 623 Doctors Bldg, Cincinnati
Place Chicago

NEW ENGLAND DERMATOLOGICAL SOCIETY

J Harper Blaisdell, President, 83 Marlborough St, Boston
Bernard Appel, Secretary, 483 Beacon St, Boston

NORTHERN NEW JERSEY DERMATOLOGICAL SOCIETY

N B Heller, President, 31 Lincoln Pk, Newark
C C Carpenter, Secretary, 38 Waldron Ave., Summit
Place Academy of Medicine of Northern New Jersey, Newark Time Third
Tuesday of March, April, October and December

SOUTHEASTERN DERMATOLOGICAL ASSOCIATION

Howard King, Chairman, 328 Doctors Bldg, Nashville, Tenn
J Lamar Callaway, Secretary, Duke Hospital, Durham, N C

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Howard Hailey, Chairman, 107 Doctors Bldg, Atlanta, Ga
John H Lamb, Secretary, 117 N Broadway, Oklahoma City

STATE

CALIFORNIA MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, DERMATOLOGY AND SYPHILOLOGY SECTION

H J Templeton, Chairman, 3115 Webster St, Oakland
Frances Torrey, Secretary, 123 Pemberton Pl, San Francisco

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Ralph E McDonnell, Chairman, 158 Whitney Ave, New Haven
Louis O'Brasky, Secretary, 1172 Chapel St, New Haven

FLORIDA SOCIETY OF DERMATOLOGY AND SYPHILOLOGY

Alan D Brown, Chairman, 117 W Duval St, Jacksonville
Lauren M Sompayrac, Secretary, 117 W Duval St, Jacksonville

LOUISIANA DERMATOLOGICAL SOCIETY

M T Van Studdiford, President, 912 Pere Marquette Bldg, New Orleans
R A Oriol, Secretary-Treasurer, 921 Canal St, New Orleans

MASSACHUSETTS MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

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J H Swartz, Secretary, 371 Commonwealth Ave, Boston

MEDICAL SOCIETY OF THE STATE OF NEW YORK, SECTION ON DERMATOLOGY AND SYPHILOLOGY

H Bauckus, Chairman, 89 Bryant St, Buffalo
Eugene Traub, Secretary, 140 E 54th St, New York

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION
ON DERMATOLOGY

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Bernhard A. Goldmann, Secretary, 500 Penn Ave., Pittsburgh.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY
AND SYPHILOLOGY

Frank Menaugh, Chairman, Ford Hospital, Detroit.
Eugene A. Hand, Secretary, 801 Second National Bank Bldg., Saginaw.

MINNESOTA DERMATOLOGICAL SOCIETY

Carl W. Laymon, President, 345 Medical Arts Bldg., Minneapolis.
F. W. Lynch, Secretary-Treasurer, 317 Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

John H. Lamb Jr., President, 117 N. Broadway, Oklahoma City.
Onis G. Hazel, Secretary, 1200 N. Walker, Oklahoma City.

TEXAS DERMATOLOGICAL SOCIETY

W. A. Smith, President, 496 Orleans St., Beaumont.
Duncan O. Poth, Secretary-Treasurer, 414 Navarro St., San Antonio.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Walter Teichmann, President, 1726 I St. N. W., Washington, D. C.
Russell J. Fields, Secretary, 1726 I St. N. W., Washington, D. C.
Place: Alternate cities. Time: Third Thursday of each month.

BRONX DERMATOLOGICAL SOCIETY

Leo Spiegel, President, 241 W. 100th St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.
Time: Fourth Thursday of each month from October to May, inclusive.

BROOKLYN DERMATOLOGICAL SOCIETY

S. H. Silvers, President, 920 Bushwick Ave., Brooklyn.
M. Estrin, Secretary, 61 Eastern Parkway, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

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James W. Jordon, Secretary, 471 Delaware Ave., Buffalo.

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Herbert Rattner, President, 25 E. Washington St., Chicago.
Michael H. Ebert, Secretary-Treasurer, 25 E. Washington St., Chicago.

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Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Lawrence C. Goldberg, Secretary-Treasurer, 623 Doctors Bldg., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except July, August and September.

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Harold N Cole, President, 1422 Euclid Ave, Cleveland
Charles G La Rocco, Secretary, 669 Rose Bldg, Cleveland

DETROIT DERMATOLOGICAL SOCIETY

T H Miller, President, 1553 Woodward Ave, Detroit
Ruth Herrick, Secretary-Treasurer, 26 Sheldon Ave S E, Grand Rapids, Mich

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Thomas B Hall, Secretary, 902 Professional Bldg, Kansas City

LOS ANGELES DERMATOLOGICAL SOCIETY

Harry C Lindsay, President, 595 E Colorado St, Pasadena, Calif
Saul S Robinson, Secretary, 1930 Wilshire Blvd, Los Angeles
Time Second Tuesday of each month, October to May, inclusive

MANHATTAN DERMATOLOGIC SOCIETY

J Frank Fraser, Chairman, 115 E 61st St, New York
Anthony C Cipollaro, Secretary, 40 E 61st St, New York

MONTREAL DERMATOLOGICAL SOCIETY

L P Ereaux, President, 1390 Sherbrooke St W, Montreal, Canada
Paul Poirier, Secretary, 456 Sherbrooke St E, Montreal, Canada

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

E William Abramowitz, Chairman, 853-7th Ave, New York
Lewis B Robinson, Secretary, 102 E 78th St, New York

NEW YORK DERMATOLOGICAL SOCIETY

Edward R Maloney, President, 80 W 40th St, New York
J Gardner Hopkins, Secretary-Treasurer, 630 W 168th St, New York

OMAHA DERMATOLOGICAL SOCIETY

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Donald M Pillsbury, Secretary, 133 S 36th St, Philadelphia
Time Third Friday of each month from September to May, inclusive

PITTSBURGH DERMATOLOGICAL SOCIETY

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Time Third Thursday of every month except July and August

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Martin F Engman Jr, President, 3720 Washington Blvd, St Louis
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Place Barnard Free Skin and Cancer Hospital Time 2 p m, second Wednesday of each month

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Frances A Torrey, President, 123 Pemberton Pl, San Francisco
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Time Third Friday of February, April, September and November

OCCUPATIONAL LEUKODERMA

EDWARD A. OLIVER, M.D.

CHICAGO

AND

LOUIS SCHWARTZ, M.D.

AND

LEON H. WARREN, M.D.

WASHINGTON, D. C.

In May 1939 an insurance company requested the examination of a group of men employed in a tannery near Chicago. These men had instituted suit against the tannery, claiming that a peculiar depigmentation of the skin, which had developed on their forearms and hands, was the result of wearing a certain type of rubber glove. A visit was made immediately to the tannery, and on the first day 20 of these men were examined. All of them showed this unusual type of depigmentation, some more than others. Thirteen of them were Negroes, 3 were Mexicans and 4 were white. In 7 of the Negroes and in 2 of the Mexicans the depigmentation was especially evident, extending over the backs of the hands and up the forearms, ending in an abrupt line halfway up the forearms. The involved areas corresponded with those covered by a heavy rubber gauntlet type of glove they had been wearing (fig. 1). In these cases the areas of leukoderma were milky white, in striking contrast to the dark skin of the Negroes. The contrast was not so great in the lighter-skinned Mexicans and was much less in the white men. Even in the most pronounced cases the palms and the dorsal aspects of the terminal phalanges of the fingers were unaffected.

In 6 of the other Negroes the depigmentation was irregular, occurring in streaks and spots, and in 1 of these there were only definite rims about $\frac{3}{4}$ inch (1.9 cm.) in width on the forearms where the upper ends of the gloves touched (fig. 2). When questioned about this he stated that after he had worn his gloves several months he had experienced some itching and irritation of the skin in these areas and had never worn them again.

Read at the Sixty-Third Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., June 1, 1940.

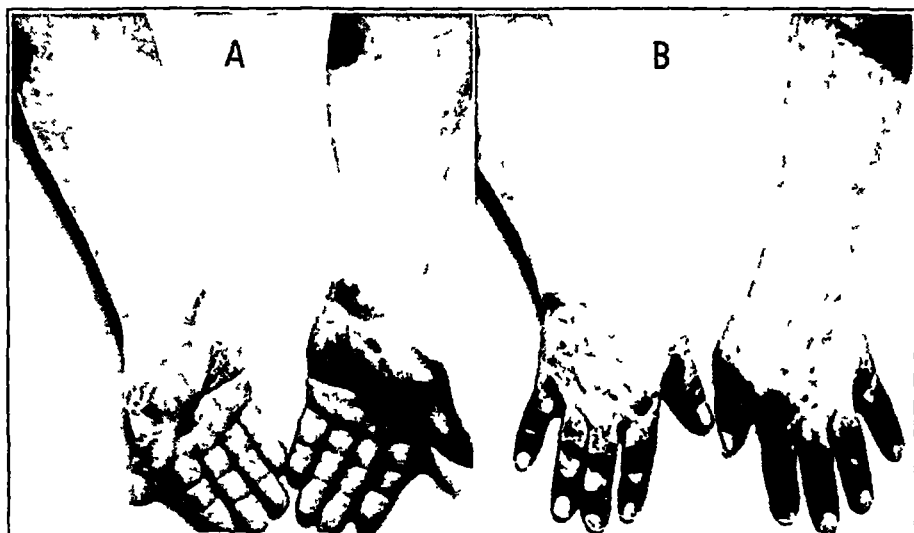


Fig 1—Leukoderma of the forearms showing (A) absence of involvement of the palms and (B) absence of involvement of the dorsal aspect of the fingers



Fig 2—Rims on the forearms at the upper margin of the gloves in a patient who discarded the gloves after wearing them for a short time

Three of the Negroes showed patches of depigmentation in the region of the biceps, the result of flexing their gloved arms against the biceps. One patient had several small patches on the right side of his face, the result of wiping perspiration away from his glasses. One man showed striking depigmentation (fig. 3) on the abdomen, upper part of the thighs and buttocks. This could not be explained except that it was possibly due to rubbing sweat and water off his body.

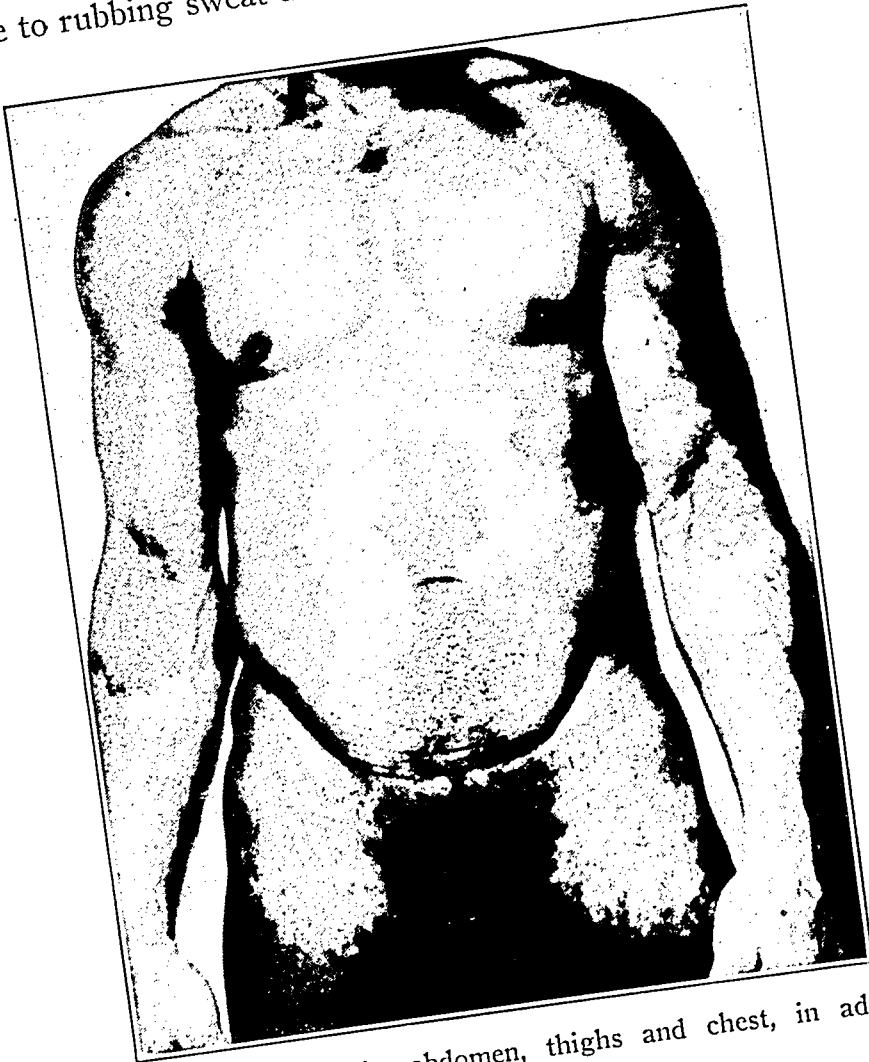


Fig. 3.—Involvement of the abdomen, thighs and chest, in addition to the involvement of the forearms.

The skin of none of these men showed signs of acute or chronic dermatitis in any of the leukodermic areas. In some cases the hair had disappeared, and in others it was short and stubby as if it had once been removed and had grown back. In a few instances it was unaffected. None of the hairs were depigmented. As these men were constantly in contact with chemicals used in the tanning of leather, it was felt that these chemicals could have been responsible for the depilation. An additional interesting feature was the behavior of the hair follicles. The

pigment about them seemed the last to disappear and the first to reappear (fig 4)

These men were intelligent and answered questions readily. Some said their leukoderma had been preceded by itching and the development of a mild dermatitis, others said they had not noted any irritation or itching. All of them stated the belief that the rubber gloves were the cause of their troubles, but as they were constantly in contact with



Fig 4—Absence of follicular involvement, pigmentation still remains about the follicles

irritating chemicals, it was our opinion that the problem required careful study.

The office of the Dermatoses Investigations of the United States Public Health Service had received a report of these cases and had already been approached by the Department of Leather Research, by the representatives of the rubber company who manufactured these gloves and also by another tannery at which the employees had a similar type of depigmentation.

An investigation was begun immediately in tannery 1. Only 48 employees out of a total of 88 employed in four departments wore the rubber gloves. Of the 48 who wore the gloves, 25 (52 per cent) had leukoderma. Ten men of 11 employed in the tan house wore gloves, but only 6 had leukoderma, a percentage of 60. Of 4 workers in the hand finishing department, only 2 wore gloves, and both of them were affected. Thirteen of 16 employed in the color and fat liquor departments wore gloves, and 7 of these had leukoderma, a percentage of 54. Only 22 of 57 employees of the beam house wore gloves, but only 9 of them had leukoderma, a percentage of 41. The janitor who cleaned the plant also wore gloves and had leukoderma.

In commenting on the presence of leukoderma in some and its absence in others engaged in the same type of work, a foreman expressed the belief that time was a considerable factor. The men worked for odd periods of time, and he had noted that those who wore the gloves the longest were the most severely affected. Personal susceptibility undoubtedly was also a factor.

Because of this we felt that possibly the p_H of the skin might vary in some of them and be a contributing factor. Eleven of the affected men and 11 unaffected were tested. The location of the test was the chest in 6 cases and the forehead in 5. The p_H of the skin of all but 1 of the affected men was 5.0 to 5.7; in 1 case the p_H was 5.9 to 6.1. Three of the men most severely affected perspired little as compared with the others. In 11 unaffected workers, 4 of whom did not wear gloves, the p_H was 5.9 with 2 exceptions; in 1 it was 4.7 and in the other 5.0. From these tests it would seem that the p_H of the skin played no part as an etiologic factor.

The employees had made so many complaints to the management about a curved finger glove, no. 62, which they had been wearing since April 1937 that they discontinued using it, thinking it was the cause of the trouble. A straight finger glove, no. 6, which had always been used up to April 1937, was substituted, and the men were apparently satisfied that they had removed the source of their leukoderma.

When we looked about for further clues, it was learned that dimethylamine was used as an unhairing agent. Since this chemical is not commonly used in tanneries, it was suspected that it might have been an etiologic factor, but this idea was abandoned when a second tannery was visited. The same type of leukoderma had developed here, but dimethylamine had never been used as an unhairing agent, and only one type of glove was used, the straight finger, no. 6, glove. A third tannery was then visited, and it was discovered that here dimethylamine was not used, that both curved and straight finger gloves were being worn

and that leukoderma developed in workers who wore either kind of gloves for any length of time

To ascertain whether this type of leukoderma occurred only in tanneries, the names of various manufacturing companies where these gloves were used were obtained from the jobbers of the gloves, and these factories were visited. These included factories where electrical apparatus and decalcomanias were manufactured, electroplating works and meat packing plants. In all of these plants the workers who wore this brand of glove were affected with leukoderma.

An important clue was obtained by the insurance company from the rubber company in a letter of June 29. In this it was stated that, whereas these gloves had been manufactured for years, in September 1937 the formula had been changed slightly by the addition of a certain material designed to improve the aging properties of the rubber.

The company was then visited, samples of the gloves were shown and samples of the aging material obtained. This was an antioxidant known under the trade name of *agerite alba*, which was said to be monobenzyl ether of hydroquinone, containing less than 1 per cent of unchanged hydroquinone. The commercial product is a light tan powder with an aromatic odor, melting at 115 to 120 C and having a specific gravity of 1.26. The pure product is white, very slightly soluble in water, practically insoluble in petroleum hydrocarbons but soluble in alkalis and benzene and in rubber up to 2 per cent. It is said to be nontoxic on ordinary handling, is nondiscoloring in diffuse daylight and gives a minimum discoloration in direct sunlight. For these reasons it is recommended by the manufacturers for use in white and light-colored gloves. The other ingredients used in the manufacture of the gloves were as follows:

Smoked sheet rubber	100 parts
Chrome yellow	5 parts
Whiting	125 parts
Cumar	3 parts
Stearax beads	10 parts
A small amount of soapstone and <i>agerite alba</i>	0.5 parts

These ingredients are mixed in a mix mill, and the mixture is rolled into thin sheets. The sheets are cut up into small pieces and placed in metal drums containing petroleum naphtha. There are 7 parts of naphtha to 1 part of compounded rubber. The drums are revolved for about forty-eight hours, after which time the rubber is completely dissolved. The solution is then pumped into a storage tank, from which it is allowed to run into the dipping vats. Porcelain forms are dipped into the solution in the vats and allowed to remain for a short time. The rubber

depositing on the forms is allowed to dry, and then the forms are dipped repeatedly until the desired thickness of rubber is obtained. After drying, the rubber is cured (vulcanized) by immersion in a 4 per cent solution of sulfur monochloride in benzene. The gloves are again allowed to dry, taken off the forms and turned inside out, and the process is repeated. After this they are dusted with soapstone.

Samples of all of the ingredients used in the manufacture of these gloves were obtained from the rubber company, and the affected workers in tannery 1 were given patch tests. Ten men were tested with (1) chrome yellow, (2) stearex, (3) the antioxidant, (4) whiting, (5) soapstone, (6) cumar, (7) the antioxidant and (8) pieces of a new acid-cured rubber glove made by the rubber company. The patches were allowed to remain on for seven days. All of the workers except 1 reacted to patches 3 and 7. It is possible that this 1 may have lost the patch from under the adhesive plaster. There was a slight reaction to patch 8, a piece of rubber glove which contained only traces of the antioxidant.

On July 24, two weeks after the patches were applied, there were signs of leukoderma at the sites of the patch tests with the antioxidant in 5 of these workers. On Jan. 25, 1940, 8 of the 10 workers were seen, and 3 of them who had shown no leukoderma on July 24 now showed leukoderma at the site of the original antioxidant patch. At the same time areas of leukoderma produced by the patch test had been repigmented in 2 of the workers.

To determine whether the tanning liquors containing these chemicals had some effect on the ingredients in the rubber by producing new compounds and in this way causing leukoderma, pieces of the rubber glove used in patch test 8 were dipped into the various tanning liquors and applied as patch tests on 6 other workers who had leukoderma: (1) a 1 per cent solution of dimethylamine; (2) the actual unhairing solution of dimethylamine and lime (as this unhairing solution is strongly alkaline and therefore caustic, the alkalinity was reduced to p_H 11 by the addition of a few drops of sulfuric acid); (3) the tanning solution (a green liquid consisting of about 1.5 per cent of chromium sulfate and sufficient sulfuric acid to give it a p_H of 3.3), and (4) the liquid expressed from the leather taken out of the fat liquor drums and consisting of remnants of the various dyes and oils used in the fat-liquoring process.

These patches were taken off each day, and the skin was inspected. The patches were remoistened with the liquors and then reapplied for seven days. There was no reaction under any of the patches at the end of the week. Seven days later, one of the men, the janitor, had a mild reaction under each of the four patches. No leukoderma developed at the site of the reactions, showing that the tanning liquors apparently did

not act on the chemicals in the rubber gloves in such a way as to change their chemical composition and produce leukoderma

To determine whether acid curing affected the action of the antioxidant and caused leukoderma, it was decided to make patch tests on all the workers with twelve samples of vulcanized rubber in its various stages of manufacture. The rubber company prepared these samples. By that time, however, it was evident that the antioxidant was the cause of the leukoderma, and the idea was dropped.

We felt, however, that tests should be made with hydroquinone, because Oettel¹ had performed experiments with it in connection with its contemplated use as a food preservative. During the course of these experiments he fed cats daily doses of hydroquinone and observed that among other changes of chronic hydroquinone poisoning there was depigmentation of the hair and black cats were temporarily changed into gray cats.

Patch tests were made on 4 of the tannery workers and 4 clinic patients, all Negroes, with a 20 per cent ointment of hydroquinone in benzonated lard. No positive results were seen.

Twenty-five workers were then given patch tests with vulcanized rubber containing nothing but 1 per cent of the antioxidant. At the end of a week, the rubber patches were removed and 22 of the men were reexamined. Four of them showed positive reactions at the site of the rubber patches, and 1 of the 4 showed a desquamation of the skin underneath which was a definite area of leukoderma. In 1 of the 3 who did not have leukoderma at the time the patches were removed, leukoderma developed at the site of the test two weeks afterward. Two had ill defined leukodermic spots, and 2 showed brown scaling. On final examination, on Jan 25, 1940, 12 of 19 of the original 25 workers given patch tests with the vulcanized rubber showed leukoderma at the site of the patch test.

In a second tannery the same experiments were performed on 4 workers. Patch tests were made with the unvulcanized rubber, an ointment of 20 per cent hydroquinone in benzonated lard was rubbed into an area on the back, and a saturated solution of hydroquinone in ether was applied to a similar area. The rubber was kept in contact with the skin for seventy-two hours, and the ointment and the ether solution were applied for four days. There were no reactions, and no leukoderma developed in the patients treated with hydroquinone, but five months later 2 of the patients who had been given patch tests with the unvulcanized rubber showed areas of depigmentation at the site of the patch tests.

1 Oettel, H. Die Hydrochinonvergiftung, Arch f exper Path u Pharmacol 183 319-362, 1936

Later 2 clinic patients were given a 20 per cent ointment of hydroquinone in benzoinated lard, and 2 patients were given a 20 per cent ointment of agerite alba in benzoinated lard; all were instructed to rub the ointment in thoroughly every night and then cover the anointed area with gauze. This was persisted in for six weeks, during which time the patients were inspected once a week. No dermatitis ensued, nor did leukoderma develop in the anointed areas. Two volunteers were then given a 50 per cent ointment of agerite alba. These patients rubbed a small amount of this ointment into one spot on their thighs for four weeks, covering the skin with a piece of gauze after each inunction. They were examined weekly for the first month and then biweekly for two months, but no dermatitis or leukoderma developed in either case.

Two volunteers were then given patch tests with agerite alba powder. A small amount was moistened, applied to a piece of gauze and strapped to a small area on the thigh. This patch was allowed to remain on the skin for a week, and at the end of the week a new patch was applied. At the end of two weeks the patch was permanently removed and the skin inspected. No dermatitis was present at that time, but two weeks later definite leukoderma began to appear; a week later the areas on 1 patient were definitely depigmented (fig. 5). In the case of the second patient leukoderma did not appear until four weeks after the removal of the patch.

The first patient was then given an ointment of 75 per cent agerite alba in hydrous wool fat. This was applied to a small area on the leg every night. In three weeks after beginning these applications the affected area was dry; the skin appeared shiny with slight desquamation, and there was partial depigmentation. One week later there was complete depigmentation in the area, and this has persisted to date (fig. 6).

The agerite alba powder was then dissolved in alcohol and collodion, and the solution was painted on one small area of the patient's left leg every night, the collodion from the previous painting being removed before the paint was reapplied. In two weeks there was the same glistening appearance of the skin at the tested site, and a slight amount of desquamation. There was no pruritus, but a week later definite depigmentation was seen.

These experiments showed that the antioxidant in rubber, in powder form, in alcohol, ether and collodion and in 75 per cent strength in an ointment base is capable of producing definite depigmentation of the skin if applied daily for two to four weeks. In 1 patient in the area treated with the powder the pigment began to show signs of returning in four to six weeks; in the other there was still some depigmentation after five months. It would also seem that the small percentage of hydroquinone present played no part in the depigmentary process.

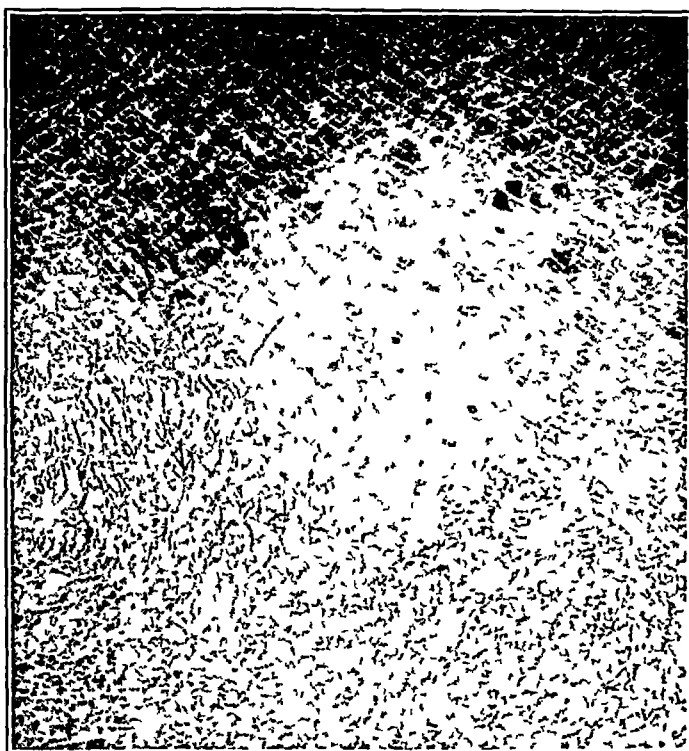


Fig 5—Positive result of a patch test with agerite alba in powder form

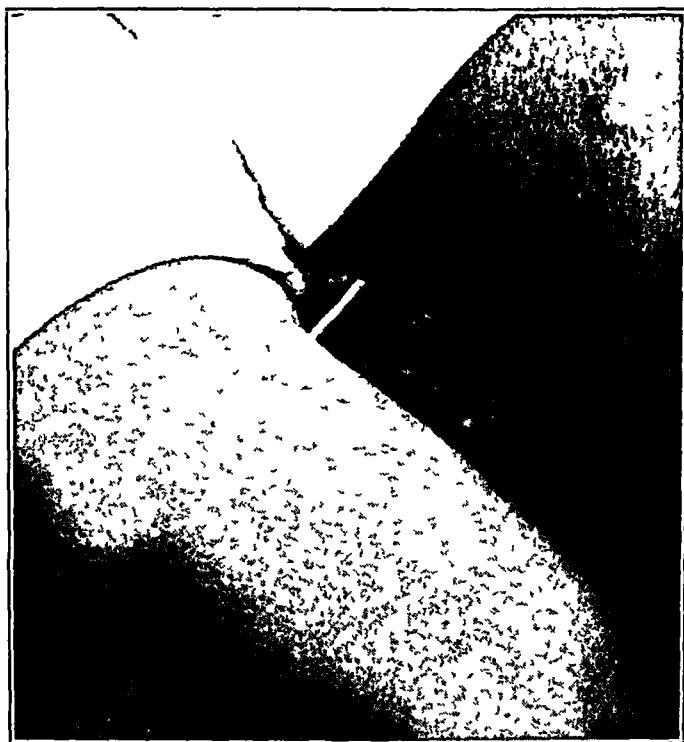


Fig 6—Right leg tested with 75 per cent agerite alba in an ointment, left leg tested with 20 per cent agerite alba in an alcohol, ether and collodion mixture,

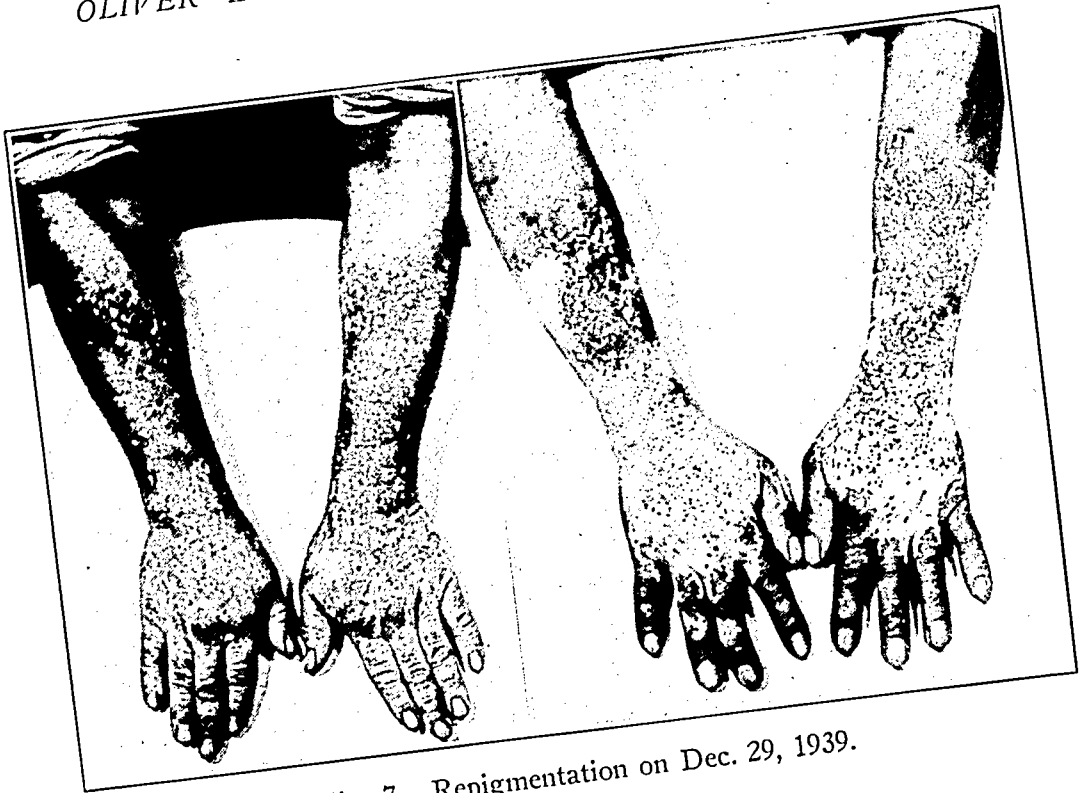


Fig. 7.—Repigmentation on Dec. 29, 1939.

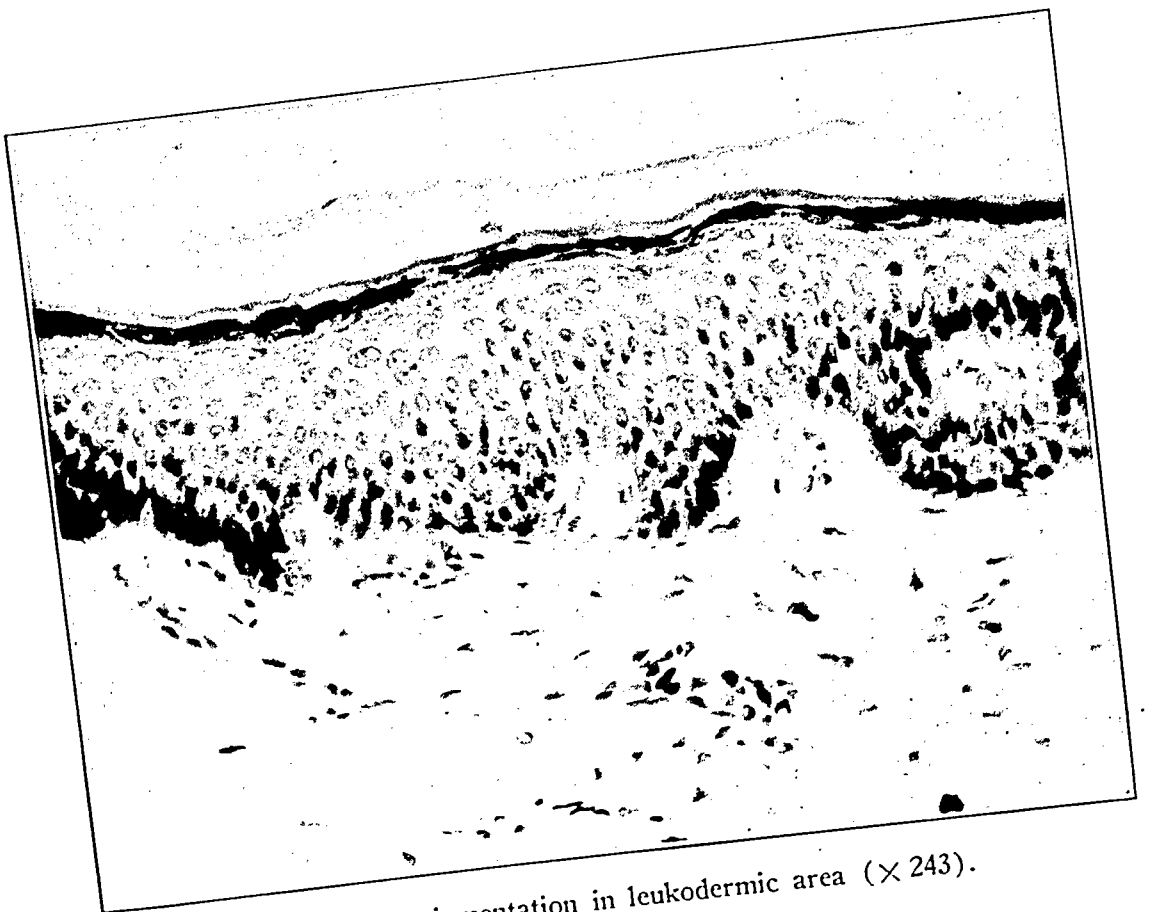


Fig. 8.—Repigmentation in leukodermic area ($\times 243$).

Repigmentation in the affected areas began in nearly all of the depigmented workers shortly after they discontinued wearing the offending gloves, and when these patients were last seen repigmentation had progressed to a remarkable degree (fig 7). In a few cases, however, it was slow. This may be another instance of personal susceptibility.

To determine whether the action of the drug on the skin was accompanied by any deleterious effects on the men's general condition, complete examinations of the blood, including reticulocyte counts and Wassermann and Kahn tests, were made for 18 patients. One Wassermann reaction was strongly positive, but other than this the results of examination of the blood were within normal limits.

Biopsy specimens were taken from the left arm, mostly from the upper margin of the affected areas, from 3 of the Negroes, 1 Mexican and 1 white man. Two specimens were taken from each person, one including normal and adjoining depigmented skin and the other including repigmented areas, particularly the follicles and the surrounding depigmented skin. These were stained with the ordinary stains and with the dopa reagent. A section of an area of repigmentation stained with the dopa reagent (fig 9) was examined by Dr. Fred Weidman, who reported as follows:

There is slight hyperkeratosis in one portion of the section. Acanthosis is negligible. Pigmentation is spotty in distribution and extreme in degree along a certain short extent of the epidermis. In the stratum corneum and in the stratum granulosum the pigment has tended to accumulate in a way that does not appear consistent with the amount of pigment in the basal layers, giving a distinctive appearance. In the deeply pigmented foci pigmentation is greatest in the basal cell layer, with marked hyperpigmentation in the chromatophores in the tips of the dermal papillae. In the less pigmented areas there is also hyperpigmentation in these chromatophores. In general, there is no marked hyperpigmentation in the basal cell layer. The localization or distribution of the pigment is utterly irregular, but even where the pigmentation is not heavy there are fine granules of pigment in the intercellular spaces. The dendritic cells are sharply outlined by powdery grains of pigment in their stellate processes, which extend far up into the epidermis. In all cases the pigment is extremely fine and powdery.

Interpretation of the Pigmentation. The primary activity is in the chromatophores, which are present even around the sweat glands but are most abundant in the tips of the papillae and in the blood vessels of the subpapillary layer. The dendritic cells in the epidermis have engulfed this pigment, thus accounting for its transportation upward into the epidermis. A rather unusual phenomenon is this accumulation of pigment in the stratum granulosum and to a somewhat lesser extent in the stratum corneum. The basal cells themselves are not the site of this production of pigment. Pigmentation in the basal layer is due more to the intercellular location of the pigment. However, there are still small quantities of pigment in the cytoplasm. The corium has a diffuse tingeing of the collagen bundles in addition to the granules of pigment. In the sweat glands the cytoplasm of the secretory cells in particular, and to a less extent of the collecting ducts, contains excessively finely granular, powdery pigment. The nuclei are not com-

promised except where the pigment is particularly dense, in which case the nucleus is somewhat pyknotic. There are no hair follicles or sebaceous glands in this section. Even the involuntary muscle around the sweat tubule is stained a diffuse brown. The arrectores pilorum muscles and also the involuntary fibers in the vessel walls have escaped involvement. In the lumens of the sweat glands is a rather shreddy, diffusely brown tinted material with some granules. One peculiar feature is the "backing up" or retention in the stratum granulosum of the pigment.

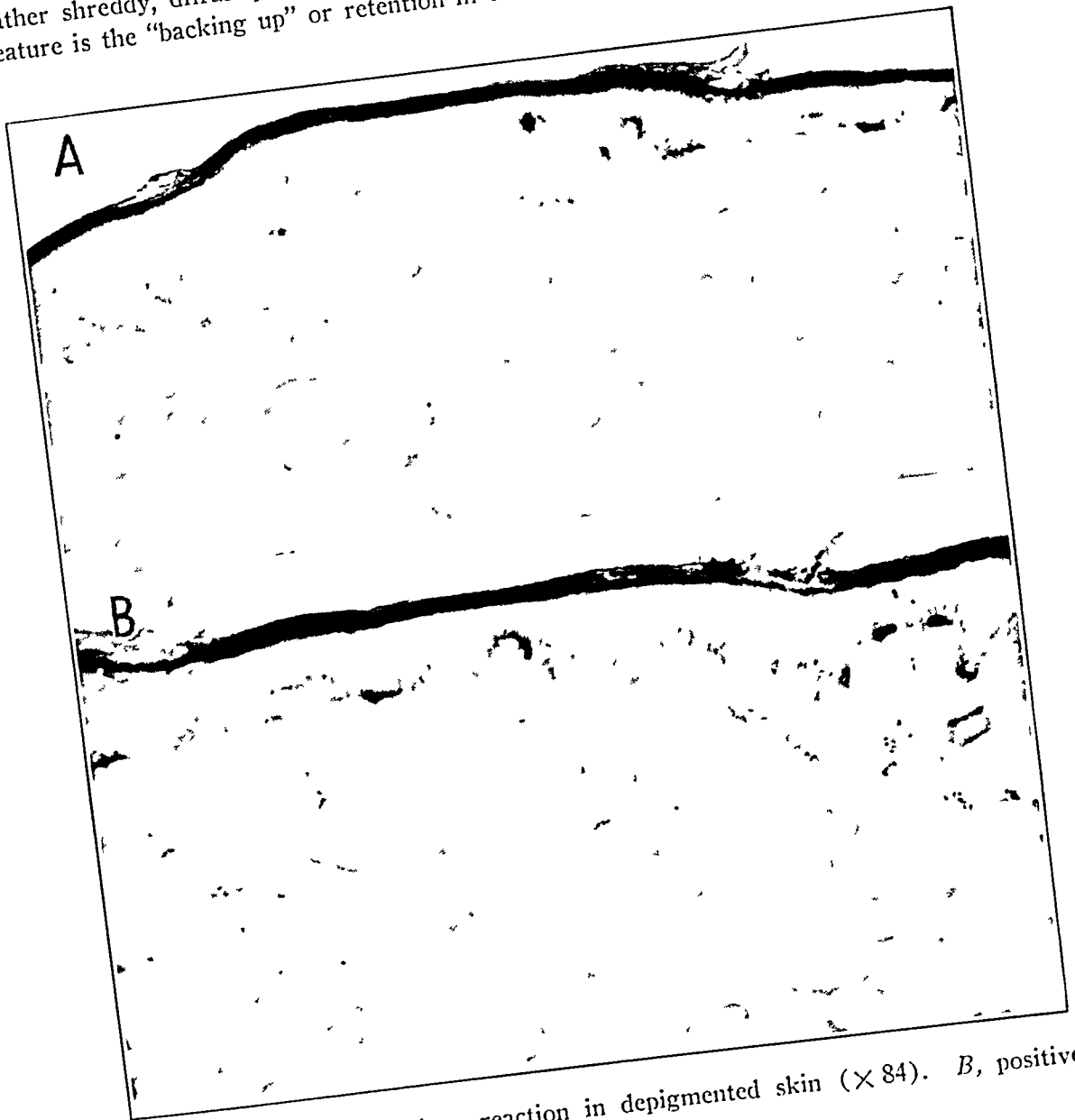


Fig. 9.—*A*, negative dopa reaction in depigmented skin ($\times 84$). *B*, positive dopa reaction in repigmented skin ($\times 140$).

A second section shows the same picture as the first, but the area of intense hyperpigmentation is more extensive. There is a lymphocytic proliferation around one blood vessel. There is a marked number of chromatophores in the tips of the derma papillae. The pigment is intercellular in the basal layer and is evidently located in the dendritic processes. The cells of the sweat gland give a positive dopa reaction, as noted in the first section, but there are no grains of pigment in these cells.

Summary The melanin pigment is present in the chromatophores which occupy the dermal papillae and in the intercellular spaces of the basal layer of the epidermis. There are also small quantities of pigment within the cytoplasm of the basal cells. The dopa reaction brings out (in addition to the observations with hematoxylin and eosin staining) that the cells of the granular layer of the epidermis are dopa positive. There are dopa-positive granules in the stratum corneum and in the secretory cells of the sweat glands.

Several other sections of normal and of depigmented areas were examined by Dr. J. W. Miller, of the United States Public Health Service, who reported as follows:

Normal skin and area of leukoderma Sections treated with dopa reagent show a rather sharp demarcation between the area of leukoderma and that of normal skin. There is a gradual decrease in the number of particles of pigment in the cells of the basal layer as the leukodermic area is approached. Dopa-positive particles occur in cells of the stratum granulosum and of the sweat glands, as intracellular and extracellular particles in the dermis and as isolated particles in the stratum corneum.

Dopa-positive particles are found in the pigmented basal cell layer of the normal portion of skin in the section. At the junction between the area of leukoderma and the normal skin there is a preponderance of dopa-positive particles in the last four or five cells before a sharp line of demarcation. Dopa-positive particles do not occur in the basal layer of the area of leukoderma, but they are noted in the dermis of the nonpigmented area, both isolated and some apparently in cells.

The same tissue stained with hematoxylin and eosin shows a similar sharp line of demarcation between the pigmented and nonpigmented cells of the basal layer, but the last few cells of the pigmented portions contain fewer particles of pigment than do the adjacent cells in the normal pigmented portion. Particles of melanin appear throughout the dermis in both portions of the section. Other than an absence of pigment, no pathologic changes are noted.

SUMMARY AND CONCLUSIONS

✓ A peculiar leukoderma occurring among 20 men employed at a tannery who wore a heavy gauntlet type of rubber glove is reported.

After a thorough investigation, including patch tests of all the affected persons, it was discovered that an antioxidant added to the rubber for the purpose of improving its aging properties was the cause.

This antioxidant is known by the trade name ageite alba and is said to be the monobenzyl ether of hydroquinone.

Patch tests made on volunteer subjects with the rubber and with the antioxidant in powder form, in a 75 per cent ointment and in a 20 per cent solution of alcohol, ether and collodion gave positive reactions in 2 cases.

Tanning liquors played no part in the depigmentation, as investigation of all plants where this brand of gloves was worn showed the same type of leukoderma among the workers.

The action of the drug on the skin had no apparent effect on the general health of the persons, as the results of examinations of the blood were within normal limits.

Biopsy specimens of the depigmented and repigmented skin stained with the dopa reagent showed the dopa reaction to be negative in the depigmented areas and positive in the repigmented ones. There was no apparent injury to the cutaneous cells.

Repigmentation in many persons began soon after they ceased wearing the affected gloves.

Antioxidants have been used in rubber for many years, but never before has leukoderma been reported from the wearing of rubber goods. Therefore, it seems that monobenzyl ether of hydroquinone has a physiologic action on the skin that other antioxidants do not have. At present we are unable to say how this drug acts on the pigment of the skin. It apparently prevents the formation of melanin, either by action on the cells which form melanin or by action on one or more of the intermediate products in the formation of melanin from the aminoacid tyrosine. Since there is no definite evidence of damage to the cells, the latter theory seems the more likely.

ABSTRACT OF DISCUSSION

DR. LOUIS SCHWARTZ, Washington, D. C.: I should like to explain some of the uses of antioxidant in rubber and the reason they are used.

Rubber tends to deteriorate rapidly when exposed to the air; in other words, it combines with oxygen. It is a familiar fact that years ago stethoscope tubes turned hard and brittle. This was because antioxidants were not used in the manufacture. Rubber now lasts much longer than it used to, owing to the use of antioxidants.

Antioxidants, or age resisters, as they are called, are compounds which have such a strong affinity for oxygen that they are able to take up nearly all of the oxygen which ordinarily might combine with the rubber. In other words, the action of an antioxidant in rubber is to combine with whatever oxygen there may be in the rubber. Antioxidants will not prevent deterioration of rubber forever, but they will delay the process.

There are many antioxidants on the market, all labeled by different trade names. The trade name agerite alba, for instance, is one used by the Goodrich Tire and Rubber Company. Agerite is a part of the trade name that is applied to all of their antioxidants (probably fifteen or twenty compounds). Some are known as agerite white, some as agerite gel and some as agerite powder. The chemical name of agerite alba is monobenzyl ether of hydroquinone, a derivative of hydroquinone.

The mode of action of antioxidants in rubber is not well understood. One theory is that the antioxidant, having a stronger affinity for oxygen than has the rubber, becomes oxidized before the rubber. The fact that antioxidants in rubber lose their action after a time seems to substantiate this theory. Another theory is that, although the antioxidant takes up the oxygen to which the rubber is exposed, it rapidly gives it up in an inactive form. If this were entirely true, the action of the

antioxidant would last indefinitely. A third theory is that the mere presence of the antioxidant in the rubber prevents the oxidation of the rubber, although the antioxidant itself is not acted on. In other words, it acts like a negative catalyst. If this theory were so, the presence of the antioxidant would again prevent the rubber from deteriorating at all.

The fact that the antioxidant is used up in the rubber is proved by experiments which show that more antioxidant can be recovered from newly compounded rubber than from old rubber.

The products of oxidation of the ordinary antioxidants are dark-colored compounds, but the oxidation product of monobenzyl ether of hydroquinone is much lighter in color.

Rubber is tacky and cannot be used without being cured. The curing of rubber removes the tackiness and gives it proper stretch and the proper comeback from the stretch. Curing is done by heat or by chemicals. Heat can be applied in either dry form or moist. The chemical used is usually sulfur monochloride dissolved in benzene or in carbon disulfide. The heat cure does not affect the action of antioxidants on rubber, nor does it seem to affect their chemical composition. The acid cure, however, causes rapid changes of color with most antioxidants, because most antioxidants are attacked by active chlorine compounds. In other words, sulfur monochloride oxidizes the ordinary antioxidants. The acid cure, however, does not affect monobenzyl ether of hydroquinone as much as it does most other antioxidants and does not cause it to discolor. This is why this antioxidant is used in light-colored, acid-cured rubber goods.

Antioxidants have been used in rubber for many years, as Dr. Oliver has mentioned, but never before has leukoderma been reported from the wearing of rubber gloves. Therefore, it seems that either monobenzyl ether of hydroquinone has a physiologic action on the skin different from other antioxidants or other antioxidants do not act on the skin.

The reason that monobenzyl ether of hydroquinone causes leukoderma and that leukoderma has not been reported to have been caused by other antioxidants may be that this antioxidant is more soluble in water and, hence, more readily absorbed into the skin. It is freely soluble in alkalis. Most of the workers who had leukoderma from the wearing of rubber gloves worked with alkalis, and the antioxidant may have been dissolved from the rubber and allowed to come in contact with the skin in an absorbable state.

It was first thought that perhaps there was an excess of monobenzyl ether of hydroquinone in the rubber, which caused the excess to bloom out and come in contact with the skin and thus be absorbed. But an examination by competent rubber chemists of the rubber gloves containing it did not show any bloom.

It was then thought that perhaps the antioxidant was dissolved out of the rubber by the perspiration. To test this, a piece of the rubber glove containing monobenzyl ether of hydroquinone was soaked in water containing sufficient acetic acid to give the solution a pH of 4, another piece of the glove was soaked in water containing a sufficient amount of alkali to give a pH of 8, these being the limits of the range of the pH of perspiration. It was found that after two weeks these solutions took 10 per cent of the monobenzyl ether of hydroquinone out of the rubber. This experiment showed that the perspiration, regardless of its pH , could dissolve monobenzyl ether of hydroquinone out of the rubber. It is possible that this amount of the antioxidant, being absorbed into the skin, was the cause of the leukoderma.

DR. LEON H. WARREN, Washington, D. C.: My discussion will be limited to a few words on the identity of this chemical which possesses the unique property of producing depigmentation of the human skin on local application.

The monobenzyl ether of hydroquinone ($C_6H_5CH_2OC_6H_4OH$), or parahydroxyphenyl benzyl ether, consists of hydroquinone with the upper or prime hydroxyl group changed into an ether linkage, to which is attached the benzyl radical (a benzene ring with a CH_2 group). Since the monobenzyl ether has a free hydroxyl group, it has many of the properties of hydroquinone, yet, owing to its ether linkage, it is more stable, less easily oxidized and less soluble.

Hydroquinone ($C_6H_4[OH]_2$) is a benzene ring with two hydroxyl groups, one in the prime position and one opposite in the para position. One characteristic of hydroquinone is that it forms quinone on oxidation. Quinone is a six carbon ring but not a benzene ring (instead of having alternate double bonds all the way around the ring, quinone has only two double bonds—on opposite sides—with an oxygen at the bottom and at the top of the ring). The quinoid structure is responsible for the color in many colored compounds. The monobenzyl ether of hydroquinone, owing to the fact that the prime hydroxyl group is substituted, does not form quinone or quinoid compounds on oxidation.

Monobenzyl ether of hydroquinone is much more soluble in alkalis. This, together with the fact that perspiration becomes progressively more alkaline on standing on the skin, may explain why some of the reactions to patch tests, particularly to the agerite alba powder itself or incorporated in rubber, were much more effective than applications of the same antioxidant incorporated in an ointment base or in an ether solution.

DR. EVERETT C. FOX, Dallas Texas: This paper has interested me greatly, as has a previous publication (Oliver, E. A.; Schwartz, L., and Warren, L. H.: Occupational Leukoderma: Preliminary Report, *J. A. M. A.* **113**:927 [Sept. 2] 1939), because of a patient that I have had the opportunity of observing for some time. In November 1939 this patient had some gastrointestinal upsets and was given medication for amebiasis. He was started with carbarsone, an arsenical, and diodoquin, a quinone compound (5,7-diiodo-8-hydroxyquinoline). These were given in fairly large doses on alternate weeks for eight months.

After about two or three months the patient noticed some changes in the skin. A small area of vitiligo appeared about the collar button area. It rapidly increased and was three or four times the size before medication was discontinued. Another area of vitiligo developed on the shoulder, and an area, which had not previously been present, on the right cheek, 3 by 1 cm. During that same period the hair rapidly became gray, an effect comparable to that in the experimental work on the development of the gray cat. During the same time, thyroid was being administered because of a low metabolic rate.

After eight months all medication was discontinued. The vitiliginous areas gradually or fairly rapidly improved. The area on the cheek disappeared completely; the one on the shoulder was much smaller, and the one on the neck was back to its previous, original size and area of depigmentation.

About this time Dr. Oliver's first article was available, and I had considered the possibility that some of the drugs had produced the increase in vitiligo. Diodoquin is 5,7-diiodo-8-hydroxyquinoline, a closely related compound.

Herman (cited by Wise, L., and Sulzburger, M. B.: The 1939 Year Book of Dermatology and Syphilology, Chicago, The Year Book Publishers, Inc., 1940, in an article on pigmentation changes in salamanders and trout, made this

observation "The melanin content of the skin is diminished with the use of diiodotyrosine and dihydroxyquinone. These substances seem to influence the hormonal system."

The patient in question, requiring further medication, was given carbarsone only, and pigmentation did not recur. For the past six months the treatment has consisted of thyroid alone, and the pigmentation has not recurred.

DR HENRY E. MICHELSON, Minneapolis. I merely want to heap some praise on Dr. Oliver and his co-workers because they have shown in this paper that busy, active practitioners can do research work equal to that done by laboratory workers.

DR MARION B. SULZBERGER, New York. A little less than two years ago a group of manufacturers of bleaching or antifreckle creams asked me to perform studies on their bleaches. The manufacture and sale of bleaching creams represents a big industry. I was told that there are relatively few Negroes or Negresses who reach maturity without having tried to get a few shades lighter by the use of freckle creams. So the greatest use of these creams is not to reduce the degree of freckling but to bleach dark skins. There is a large export business in these products. A great deal is sold all over Africa, for example. Almost all the best known brands of antifreckle creams are manufactured in the South.

The basis of these creams is almost always some form of mercury. Many of them contain white ammoniated mercury in 5 to 15 per cent concentration. Some of the creams contain red mercuric oxide in somewhat lower percentage. The fact that throughout the dermatologic literature and dermatologic practice mercury is the most highly vaunted and the most used bleaching agent interested me in the project of scientifically studying the effects of these mercurials on the skin. Dr. Ludwig Schwarzschild and I carried out these studies on large numbers of Negroes.

At a meeting last year Drs. Oliver, Schwartz and Warren spoke to me about their observations with *agerite alba*. I then asked permission to include this substance as an extension of some of my studies of bleaching agents. The report I am now going to make is really made possible only through the courtesy of Dr. Oliver and his collaborators and is merely supplementary to their results.

One of the questions which arose, and which Dr. Oliver also mentioned, was whether the depigmentation from application of *agerite alba* was merely an effect of irritation. It seems to be a common belief that if pigmented skin is irritated sufficiently depigmentation is likely to occur. To check this, Dr. Schwarzschild and I applied *agerite alba*, full strength, to the skin of 18 Negroes. Simultaneously, to the skin of the same Negroes we applied ammoniated mercury, full strength, and hydroquinone, full strength, in each instance using just the powder moistened and applying it in patch tests. In all cases there was decided irritation from the full strength of each of the three substances. However, at the site of the irritation due to *agerite alba* in 17 of the 18 Negroes there was depigmentation after an average of twenty-seven and one-half days. At the site of the application of ammoniated mercury there was no change in pigmentation. This site, once the irritation had subsided, could not be distinguished from the normal surrounding skin. At the site of the irritation from hydroquinone, in 8 of 12 patients not only was there no depigmentation but there was decided hyperpigmentation.

I think that the conclusion to be drawn from this experiment is obvious. *agerite alba* does not act merely by producing irritation but exercises some specific damaging or inhibiting effect on the pigment or on the formation of pigment. More-

over, this specific effect is apparently not due to the presence of hydroquinone or simply to the irritation. The nature of this specific effect of *agerite alba* requires further study.

This work, of course, not only brings up many theoretic problems, such as new possibilities of studying the genesis of pigmentation and the origin of melanin and pigment but also suggests certain eminently practical problems.

It would, of course, be of great advantage to dermatologists to possess a reliable bleaching agent which could be used with safety in topical applications to produce any desired degree of local loss of pigmentation. With this objective in mind, Dr. Schwarzschild and I continued our studies, after corresponding with Dr. Oliver, who gave us several suggestions.

Our next experiment was designed to determine whether one could reduce the irritation and still produce the depigmentation. So we embodied the *agerite alba* in various vehicles, one of them being rubber cement. In a series of 7 Negroes, the 1 per cent *agerite alba* in rubber cement produced depigmentation in 4. However, there was still irritation. In other words, the conclusion is that we have not yet been able to discover an optimum concentration or a suitable vehicle by which no irritation would be produced and with which one could regularly elicit depigmentation.

In a third experiment, we tried the concentrated *agerite alba* and also pastes of 75 per cent *agerite alba* on the skins of 5 heavily freckled white persons. No effect was noted on the freckles.

In an extension of these experiments, we tried to find out whether the degree of depigmentation was parallel with the degree of irritation produced by the *agerite alba*. It was not. In 9 cases the irritation was seen first and later depigmentation appeared; in 8 depigmentation was seen before there was any clinically visible irritation, and in 1 case, in which the skin was severely irritated by the *agerite alba* in full strength, there was no depigmentation whatever.

I believe that our results, together with those of Drs. Oliver, Schwartz and Warren, now permit conclusions which can be stated approximately as follows:

1. The depigmentation produced by the local application of *agerite alba* is not simply the result of irritation but must be the result of some specific factor acting on the pigment or on the formation of pigment.

2. This effect is not due to the presence of free hydroquinone.

There is one more point I should like to bring up. In our experiments we were able to produce eczematous, allergic, specific sensitization both to the hydroquinone and to *agerite alba*, a real allergic sensitization, such as one can produce with poison ivy extracts. In approximately 50 per cent of the cases we produced this eczematous sensitization by the application of full strength *agerite alba*. Again, however, there was no definite parallelism between the sensitization produced and the depigmentation which followed. In other words, some of the persons who became sensitized did not become depigmented, and some who did not become sensitized did become depigmented.

I should like to compliment the presenters once again. It should be appreciated that, starting with a clinical observation, which was really at first based on a merely medicolegal and economic question, Drs. Oliver, Schwartz and Warren have, by their careful approach to the problem and by their scientific attitude, been able to bring to attention something which is new and fundamental. The importance of the discovery of this new and really effective bleaching agent is amply evident in the fact that this discussion has developed into a symposium on the genesis and

chemistry of pigment, including the practical applications of bleaching agents, the effects of rubber antioxidants and the relation of oxidation and reduction ferments to the mechanism of the formation of melanin and the genesis of pigment

DR SAMUEL M PFCK, New York I wish to congratulate the presenters on this interesting work The most important point was that it has led to perhaps a new method of studying the oxidase reaction of the pigment I, too, obtained clinically the same results which have just been reported I was able to produce depigmentation in guinea pigs by local applications, but I was unable by feeding experiments to produce any changes such as have been reported as occurring in cats

Technical difficulties were encountered in experimenting directly with frozen sections, because the dopa oxidase is destroyed by ether and alcohol, while agerite alba is practically insoluble in water

It then occurred to me that the effect of agerite alba on the polyphenol oxidase in the leukocytes would lend itself well to direct experimentation, as this substance is less sensitive to alcohol and ether

A number of years ago, Bloch and I published a method of demonstrating polyphenol oxidase by means of dopa (Bloch, B, and Peck, S M *Der Nachweis der Oxydase in den Zellen des myeloischen Systems durch 3, 4-Dioxy-phenylalanin, Folia haemat* 41 166 [May] 1930), using this technic for fixation of blood smears We experimented with the effect of agerite alba in such a preparation

When a blood smear is exposed for one hour to ether prior to immersion in the dopa solution, according to the technic described by Bloch and myself, there is a negative dopa reaction in the leukocytes It would then logically follow that if a fixed blood smear were exposed to a solution of agerite alba for one hour prior to immersion in a dopa solution, a negative reaction should ensue However, when the blood smear, which has been previously fixed with formaldehyde vapor, is immersed in a 1 per cent solution of monobenzyl ether of hydroquinone for one hour, not only is a subsequent dopa reaction obtained, but it is much more strongly positive than the controlled dopa reaction In collaboration with Dr Harry Sobotka (to be published), I conducted many experiments on the various oxidase systems They substantiated the observations that agerite alba seems to increase the polyphenolase oxidase even after it has been weakened by ether

A number of allied hydroquinones were studied, such as the dibenzyl ether of hydroquinone, for their effect on the polyphenolase There was none Similarly these allied substances did not seem to act on animals as did the agerite alba

The importance of these observations lies in the fact that the monobenzyl ether of hydroquinone seems to have a sharp specific antioxydase effect on the dopa oxidase, which differs from its effect on the polyphenolase It also tends to point out the specificity of the dopa reaction Agerite alba seems to be a specific dopa oxidase poison, and this information may throw a great light on the mechanism of vitiligo

DR WILLIAM HARVEY GUY, Pittsburgh This is a noteworthy communication because of the scientific explanation of a bizarre occupational dermatosis The authors, I think, are to be particularly complimented on the fact that they have isolated the chemical at fault and have consulted the rather cooperative manufacturers with regard to changing the manufacturing process so as to avoid depigmentation in future contacts

I have had the opportunity of studying 10 such cases in Pittsburgh The condition occurred in car cleaners in the Pittsburgh Railway Company They were referred without comment, for diagnosis and explanation It was not suggested

at first that gloves might be in the background. It was first suspected that the cleaning materials that they used might be at fault. Definite reactions to patch tests could be produced but no depigmentation. Then, finally, the glove material was suspected. Patch tests with both used gloves and new gloves produced a mild erythema, usually appearing after the fourth day and more often at the end of a week. Depigmentation rarely appeared before fourteen days after the application.

A histologic section was made of tissue in the area of the positive reaction to the patch test, and rather intense edema, both parenchymatous and interstitial, was found, involving the epidermis, particularly noteworthy with reference to the basal membrane. It was difficult to note the line of demarcation between the cutis and the epidermis. Repigmentation ensued in practically all cases. But there is one point that I should like to ask Dr. Oliver and his co-workers about, and that is whether or not in their cases the repigmentation was complete. In our cases repigmentation did occur but it was not complete.

I think another point of interest and importance in connection with this presentation is the implications of the use of this antioxidant in dermatology from a practical standpoint in the future. If the substance produces permanent depigmentation, it may ultimately prove to be of some service in the removal of residual pigment, as after burns, for cosmetic results.

DR. E. B. TAUBER, Cincinnati: I want to report other types of cases. Since Dr. Oliver called my attention to this phenomenon about a year ago, I have come in contact with 4 additional cases, in which the condition had nothing to do with an occupational type of leukoderma. In 2 of these the conditions were approximately the same and were due to the rubber in dress shields. The third case was that of an obese woman who wore a rubber corset for reducing purposes and was depigmented to a decided extent after using the corset for a little less than a month. The fourth case was that of a Portuguese who had complained of pain in the buttocks and was told by his physician to apply heat; so he lay on a hot water bag for about three weeks, and a depigmented spot about the size of a palm appeared. Dr. Oliver has pictures of the 2 women. They were given patch tests with *agerite alba* and gave positive reactions. The obese woman and the Portuguese also gave positive reactions to patch tests with *agerite alba* in powder form.

There are so many other situations in which rubber comes in contact with the skin that I think one needs to be on the lookout for cases of this condition. Repigmentation has almost completely taken place in both women.

There is one fact which has not been mentioned. The depigmentation takes place in a sort of stippling way at first, and then the skin gradually becomes milky white. Repigmentation appears in the same way; little black spots come out and then fuse, and the skin finally becomes completely repigmented.

DR. FRED D. WEIDMAN, Philadelphia: I have been impressed with the remarkable consistency with which the skin around the hair becomes depigmented. In this connection, it appears that the commercialists have rendered us a great service, because they have unwittingly stumbled across a particular chemical—monobenzyl ether of hydroquinone—which is delicately specific in relation to the pigmentary oxidase. Thus, heretofore it was thought that oxidase was a single substance. However, it appears that the effect of this antioxidant is different on the cell processes from place to place.

As I see it, there are two possible explanations for this. One is that not simply one kind of oxidase is elaborated in cutaneous cells; perhaps there are

two different kinds, or perhaps even more, one of which (in perifollicular cells) is specifically affected by this particular compound while others are not

There is one other possible explanation, namely, the factor of dosage. Around the hair follicles cellular processes in general are normally more active, and therefore larger quantities of oxidase, among other products, are produced in that position. These larger quantities are not "neutralized," so to speak, by the compound, whereas in positions apart from the follicles, where cellular processes are not so active, the oxidase is not produced so rapidly, and there is sufficient dosage of the compound to neutralize the oxidase. This, of course, is theoretic. No doubt the same thoughts have occurred to Dr. Oliver and his collaborators. But definite attention should be given to the consistency of the depigmentation around the hair follicles.

DR. GEORGE M. LEWIS, New York: I should like to ask Dr. Oliver if any of the patients have shown any constitutional symptoms or any toxic side effects.

DR. EDWARD A. OLIVER, Chicago: I appreciate the generous discussion. There is little that I can add to it.

Dr. Fox's observations are most interesting. He wrote me several months ago about his patient. While the depigmentation in his case may be only a coincidence, it is known from Oettel's experiments that hydroquinone taken internally has altered the color of hair.

Dr. Guy asked about repigmentation. In most of the cases there is repigmentation, but it is a partial, blotchy type of repigmentation. In tannery 1 there are as yet no cases of complete repigmentation, with the skin showing a normal type of pigmentation.

Dr. Lewis asked about constitutional symptoms. As far as we could see, there were no constitutional symptoms. The affected men never lost any time from work.

ULCERS OF THE LEGS IN SICKLE CELL ANEMIA

CLYDE L. CUMMER, M.D.
AND

CHARLES G. LAROCCO, M.D.
CLEVELAND

In dermatologic practice ulcers of the legs often present difficulty in differential diagnosis. A Negro patient in our outpatient clinic who had had several such ulcers for many months was finally found to have sickle cell anemia. To direct more general attention to this possibility is the purpose of our communication. It is necessary first to review briefly the clinical and hematologic picture of the blood anomaly.

Sickle cell anemia was first described by Herrick¹ in 1910. It was recognized early that while many of the Negro race show sickle cells in the peripheral blood—indeed, 7.8 per cent, according to Cardozo's² recent study—by no means all of this number are anemic. This has led to confusion in terminology. The anemia, first given Herrick's name, has been called sickle cell anemia and later drepanocytic anemia, while the terms sickle cell anemia and drepanocytosis have been applied to the symptomless or nonanemic state. It is generally recognized, as has been noted by Diggs and Ching,³ that the lines between nonanemic, mildly anemic and severely anemic conditions are not sharply drawn and that clinically conditions have been observed to pass from the sickle cell phase to the active phase and back again. Therefore, there has arisen the use of the terms latent and symptomless sickle cell anemia to denote the nonanemic phase.

The sickling trait is familial and apparently hereditary, dominant in character and transmitted according to the mendelian law. Syden-

From the Department of Dermatology and Syphilology, St. Vincent Charity Hospital.

Read at the Sixty-Third Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., May 30, 1940.

1. Herrick, J. B.: Peculiar Elongated and Sickle-Shaped Red Blood Corpuscles in a Case of Severe Anemia, Arch. Int. Med. 6:517-521 (Nov.) 1910.

2. Cardozo, W. W.: Immunologic Studies of Sickle Cell Anemia, Arch. Int. Med. 60:623-653 (Oct.) 1937.

3. Diggs, L. W., and Ching, R. E.: Pathology of Sickle Cell Anemia, South. M. J. 27:839-845, 1934.

stricker⁴ concluded that more children born of parents both of whom show meniscocytosis have sickle cell anemia than those born of 1 affected and 1 normal parent

A striking feature of sickling is that it is limited almost exclusively to the Negro race. In fact, until recently it was regarded as being so limited. Sydenstricker⁴ stated that it occurred only in Negroes or in those with a strain of Negro blood. However, Haden and Evans⁵ regarded as authentic 8 examples of the disease in the white race. In each instance a careful examination had been made to exclude Negro blood. Later its occurrence in a Sicilian was reported by Pontoni⁶. Wallace and Killingsworth⁷ tested 139 Mexican children and 100 Mexican adults and found the condition in 3. On the other hand, in an examination of 2,000 white persons Sydenstricker failed to find an instance of sickling.

Sickling has been observed at all ages from infancy to 78 years, but the incidence of anemia is highest in childhood. Progressive diminution with advancing age is accounted for by excessive mortality. There seems to be no preference as to sex, as shown by the compilation of published statistics made by Diggs, Ahmann and Bibb,⁸ for in a group of 2,831 Negroes examined, 81 per cent of the females and 84 per cent of 2,252 males had the trait. There is no appreciable difference in percentage incidence in the United States between persons living in the northern and in the southern states.

CLINICAL FEATURES OF THE ANEMIC STATE

With meniscocytosis only there may be no symptoms or physical signs. With anemia the signs vary somewhat with the duration of the disease. In infants and young children there is malnutrition, and at the age of puberty retardation of development is often noted. The clinical manifestations have been described by Huck,⁹ Diggs and co-workers,

4 Sydenstricker, V. P. Sickle Cell Anemia (Herrick's Syndrome), in Christian, H. A., and Mackenzie, J. Oxford Medicine, New York, Oxford University Press, 1930, vol. 2, pt. 3, pp. 849-860.

5 Haden, R. L., and Evans, F. D. Sickle Cell Anemia in the White Race. Improvement in Two Cases Following Splenectomy, *Arch Int Med* **60** 133-142 (July) 1937.

6 Pontoni, L. Sulla eritropatia drepanocitica costituzionale tipo Herrick, *Haematologica* **20** 657-724, 1939.

7 Wallace, S. A., and Killingsworth, W. P. Sicklemia in the Mexican Race. *Am J Dis Child* **50** 1208-1215 (Nov.) 1935.

8 Diggs, L. W., Ahmann, C. F., and Bibb, J. The Incidence and Significance of the Sickle Cell Trait, *Ann Int Med* **7** 769-778, 1933.

9 Huck, J. G. Sickle Cell Anaemia, *Bull Johns Hopkins Hosp* **34** 335-344, 1923.

Sydenstricker and co-workers and others. As with all anemic states, the patient's complaints include weakness and general poor health. In order of frequency Anderson and Ware¹⁰ listed the following signs and symptoms: greenish yellow scleras, heart murmurs, enlargement of the liver, adenopathy, abdominal pain, enlarged spleen, ulcers of the leg, pulmonary disease, fever, enlarged spleen, vomiting and infantile genitalia. Adenopathy occurs chiefly in the cervical and axillary lymph nodes. Since the complaints may include pains in the joints and muscles (often regarded as rheumatism), shortness of breath and palpitation, the mistaken diagnosis of "heart disease" is occasionally made; or in the mind of the physician the joint and cardiac symptoms may be correlated and explained as evidences of rheumatic infection.

The green discoloration of the scleras frequently encountered must not be confused with the yellow of biliary jaundice or the muddy pigmentation often seen in Negroes. However, clear scleras cannot be regarded as conclusive evidence against the coexistence of sickling, since in a series of 97 Negroes with no definite scleral discoloration, Diggs, Ahmann and Bibb found sickle cells in the blood of 6.

Enlargement of the heart may be associated with a systolic apical murmur. The splenic enlargement is occasionally enormous, but there is a tendency toward atrophy as the disease advances, sometimes to such an extent that the mere remnant is not discoverable at splenectomy. The legs may show edema; ulcers and scars will be described later.

Recurrent attacks of acute abdominal pain occur not infrequently and have been emphasized by many writers on the subject, including Leivy and Schnabel.¹¹ As described by Campbell,¹² these episodes may be severe and accompanied by obstructive jaundice, fever, muscle spasm, leukocytosis, nausea and vomiting, simulating cholecystitis, appendicitis, salpingitis or ileus. Severe attacks of pains in the joints or bones may suggest acute osteomyelitis or acute rheumatic fever. Occasionally there is low grade fever.

Cerebral vascular accidents have been reported, and Bridgers¹³ stated that the disorder may manifest itself first by signs and symptoms indicative of cerebral vascular disease, leading to a diagnosis of either thrombosis or intracranial hemorrhages.

10. Anderson, W. W., and Ware, R. L.: Sickle Cell Anemia, J. A. M. A. 99:902-905 (Sept. 10) 1932.

11. Leivy, F. E., and Schnabel, T. G.: Abdominal Crises in Sickle-Cell Anemia, Am. J. M. Sc. 183:381-391, 1932.

12. Campbell, E. H., Jr.: Acute Abdominal Pain in Sickle Cell Anemia, Arch. Surg. 31:607-621 (Oct.) 1935.

13. Bridgers, W. H.: Cerebral Vascular Disease Accompanying Sickle Cell Anemia, Am. J. Path. 15:353-362, 1939.

Active sickle cell anemia appears to have a definite effect on the fertility of the female, according to Sodeman and Burch,¹⁴ for pregnancy is seldom reported in cases of the disease. They listed 1 case of their own in which the patient reached term and the baby's blood showed sickle cell anemia when first examined, six weeks after birth, and 2 other cases, previously reported by Lash¹⁵ and Sharp and Schleicher,¹⁶ in which live, full term babies were delivered. Indeed, sickle cell anemia has been regarded as a possible cause of abortions.¹⁷

PATHOLOGIC CHANGES

The following essential pathologic changes were summarized by Diggs and Ching:³ sickled erythrocytes, congestion of the capillaries, thrombi, infarcts, fibrosis, hemolytic anemia with increased phagocytic activity of the reticuloendothelial system, retention jaundice, deposits of pigment in the liver, spleen, bone marrow, lymph nodes and kidney, hyperplasia of the bone marrow, a regenerative blood picture and degenerative visceral changes. Other changes in the tissue regarded by them as noteworthy are early splenic congestion, followed by hemorrhage, infarction and fibrosis with siderotic nodule formation and late atrophy, hepatomegaly with prominent Kupffer cells, congestion, pigmentation and scarring of the kidney, cardiac enlargement, ulcers of the legs and osseous changes.

The heart is frequently hypertrophic, the hypertrophy being confined to the left side, predominantly in the left ventricular wall, and the myocardium may show slight to moderate patchy degeneration, according to Steinberg,¹⁸ who made an extensive review of the pathologic studies.

Bridgers¹³ observed that in 1 of his cases of cerebral vascular accidents the large subarachnoid vessels had undergone gradual obliteration, with final complete closure through a process identical with that which results in occlusion of the splenic arteries, while in the other the process developed in connection with the small intracerebral vessels, resulting in multiple focal necroses and hemorrhages in the brain. Diggs and

14 Sodeman, W. A., and Burch, G. E. Pregnancy in Active Sickle Cell Anemia, *New Orleans M & S J* **90** 156-158, 1937.

15 Lash, A. F. Sickle Cell Anemia in Pregnancy, *Am J Obst & Gynec* **27** 79-84, 1934.

16 Sharp, E. A., and Schleicher, E. M. Hemologic Observations on Sickle Cell Anemia, *Am J Clin Path* **6** 580-590, 1936.

17 Lewis, A. W., Jr. Sickle Cell Anemia with Pregnancy, *Am J Obst & Gynec* **33** 667-671, 1937. Yater, W. M., and Mollari, M. The Pathology of Sickle Cell Anemia. Report of a Case with Death During an "Abdominal Crisis," *J A M A* **96** 1671-1675 (May 16) 1931.

18 Steinberg, B. Sickle Cell Anemia, *Arch Path* **9** 876-897 (April) 1930.

Bibb,¹⁹ having found the small blood vessels distended by sickled cells, advanced the theory that the great length of these cells interferes with the free circulation of the blood and that this is a factor in the production of thrombosis, a common feature in this disease.

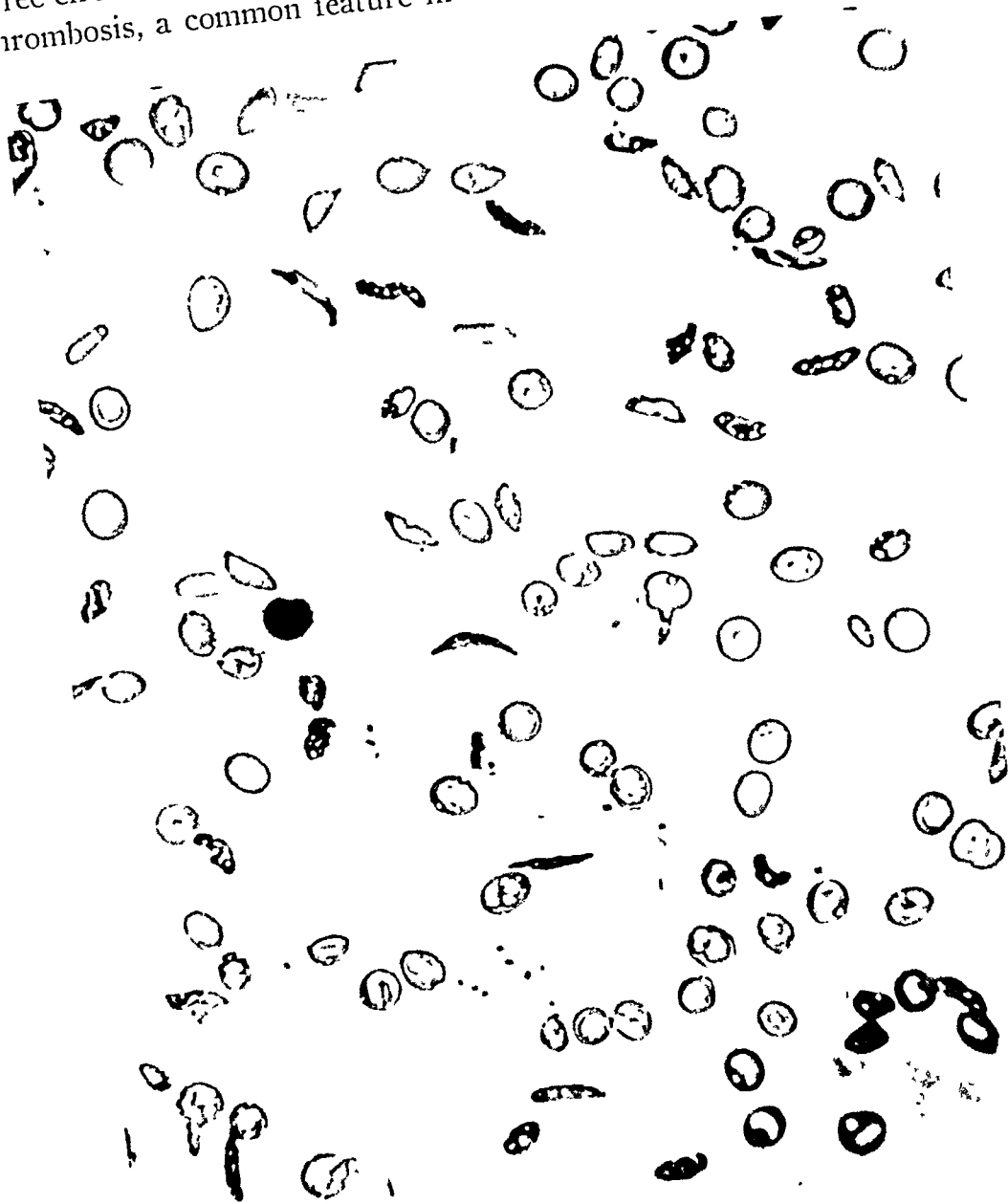


Fig. 1 (case 3).—Blood film, stained with Wright's stain, showing erythrocytes, poikilocytosis, increased central pale and occasional and sickle-shaped red corpuscles ($\times 510$).

The bone in many instances shows evid reparative processes in the marrow, the lesio infarction, necrosis, hemorrhage, granular and c

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19. Diggs, L. W., and Bibb, J.: The Erythrocyte i
J. A. M. A. 112:695-701 (Feb. 25) 1939.

linization, fibrosis, abnormal calcification and new bone formation, according to Diggs, Pulliam and King²⁰ They stated that the changes in the skull usually described as characteristic include increased thickness, absence of a well defined outer table, osteoporosis and pointed trabeculae striations radiating outward from the inner table and perpen-



Fig 2 (case 3)—Wet blood smear, sealed with petrolatum, after standing twenty-four hours, showing crescentic and oat-shaped forms ($\times 945$)

dicular to it, an abnormality not specific for sickle cell anemia, since it may be found also in erythroblastic anemia, hemolytic jaundice and other conditions. The bones of the extremities most likely to show abnormalities are the tibia and the fibula.

²⁰ Diggs, L. W., Pulliam, H. N., and King, J. C. The Bone Changes in Sickle Cell Anemia, *South M. J.* **30** 249-259, 1937.

THE BLOOD PICTURE

It was the striking appearance of the erythrocytes which first drew attention to this anomaly. The morphologic changes are best observed when a drop of blood is sealed under a cover slip and studied for hours or even days. While occasionally slender, pointed or sickle-shaped cells



Fig. 3 (case 3).—Wet blood smear, sealed with petrolatum, after standing forty-eight hours, showing elongated and multipointed forms ($\times 920$).

are seen when the preparation is first made, usually time is required for the development of characteristic shapes. The behavior of the erythrocytes in wet preparations has been fully described by Diggs and Bibb.¹⁰ While the change in the erythrocytes may begin in the first hour after the blood is obtained, usually it takes place at maximal rate in from two to six hours, and often it is complete within twelve to twenty-four

hours Erythrocytes in stained blood films resemble those found in newly made moist preparations Fish fin or multipointed shapes are not usually seen in stained films in complete form but are occasionally found on careful search ²¹

The blood has been studied by numerous investigators, including Emmel,²² Sydenstricker, Mulherin and Houseal,²³ Huck,⁹ Hahn and Gillespie,²⁴ Hem, McCalla and Thorne,²⁵ Graham and McCarty,²⁶ Sharp and Schleicher,¹⁶ Vaubel,²⁷ Haden and Evans ⁵ and, most recently, Diggs and Bibb ¹⁰

In Diggs's ²⁸ series of 72 cases the red blood cell count averaged 2,600,000 per cubic millimeter and the hemoglobin 45 per cent The reticulocyte count was usually elevated, often about 25 per cent, the percentage increasing during exacerbation and decreasing with remission, following the curve of the nucleated blood cells He found the white blood cell count characteristically increased, the average in 69 cases being 18,000 per cubic millimeter The resistance of erythrocytes to

21 The examination of the blood for sickle cells is extremely simple While hanging drop preparations of blood mixed with physiologic solution of sodium chloride are recommended by some, every practical purpose is served by placing a small drop of blood on a slide, covering with a thin cover slip and rimming the edges with petrolatum Such preparations may be kept several days for observation Sealing prevents evaporation and consequent degenerative changes in the red cells and permits them to live, exhausting the oxygen and increasing the carbon dioxide content in the plasma, which in turn accelerates the morphologic changes Fresh wet preparations should be practically free from rouleaux formation and crenation For this reason the slides and cover slips must be absolutely free from grease and lint It is helpful to cleanse them immediately before use with 95 per cent alcohol to which a small amount of ammonia has been added and to dust them off with a camel's hair brush immediately before picking up the drop of blood

22 Emmel, V E A Study of the Erythrocytes in a Case of Severe Anemia with Elongated and Sickle-Shaped Red Blood Corpuscles, *Arch Int Med* **20** 586-598 (Oct) 1917

23 Sydenstricker, V P, Mulherin, W A, and Houseal, R W Sickle Cell Anemia Report of Two Cases in Children with Necropsy in One Case, *Am J Dis Child* **26** 132-154 (Aug) 1923

24 Hahn, E V, and Gillespie, E B Sickle Cell Anemia Report of a Case Greatly Improved by Splenectomy, Experimental Study of Sickle Cell Formation, *Arch Int Med* **39** 233-254 (Feb) 1927

25 Hem, G E, McCalla, R L, and Thorne, G W Sickle Cell Anemia, with Report of a Case with Autopsy, *Am J M Sc* **173** 763-772, 1927

26 Graham, G S, and McCarty, S H Sickle Cell (Meniscocytic) Anemia, *South M J* **23** 598-607, 1930

27 Vaubel, E Die Sichelzellenanämie, *Ergebn d inn Med u Kinderh* **52**. 504-542, 1937

28 Diggs, L W The Blood Picture in Sickle Cell Anemia, *South M J* **25** 615-620, 1932

hypotonic solution of sodium chloride is variable but usually increased. The average of determinations in 25 cases of active involvement revealed hemolysis beginning in a 0.35 per cent solution of sodium chloride and complete hemolysis in a 0.22 per cent solution, although extremely low percentages have been reported by Bell, Kotte, Mitchell, Cooley and Lee²⁹ and one of 0.03 per cent by Hahn.³⁰ The hemolytic character of the anemia is confirmed by finding an increase in the serum bilirubin. The direct van den Bergh test usually gives a negative result, and the indirect, a positive result. Urobilin is present in the urine.

TREATMENT OF ANEMIA

There is no known effective treatment for sickle cell anemia. There is no response to iron or liver therapy. Splenectomy was first suggested by Sydenstricker.³¹ Ching and Diggs³² reviewed the results in reported cases and concluded that permanent benefit following the procedure had not been proved. Haden and Evans⁵ followed 2 patients for fourteen and five years, respectively, after surgical treatment but found it difficult to evaluate the efficacy of splenectomy.

ULCERS OF THE LEGS

In the first report on a patient with sickle cell anemia Herrick¹ described scars on the legs, which were said to have followed yaws, the patient having formerly resided in the West Indies. However, even on arrival in New York years afterward the patient had a sore on one ankle which left a similar scar. In the next 3 cases reported, respectively, by Washburn,³³ Cook and Meyer³⁴ and Mason³⁵ there were ulcers of the legs. Since then the occurrence of such ulcers in this condition has been noted by many in the general medical literature.

29. Bell, A. J.; Kotte, R. H.; Mitchell, A. G.; Cooley, T. B., and Lee, P.: Sickle Cell Anemia: Report of Two Cases in Young Children in Which Splenectomy Was Performed, *Am. J. Dis. Child.* **34**:923-933 (Dec.) 1927.

30. Hahn, E. V.: Sickle-Cell (Drepanocytic) Anemia with Report of a Second Case Successfully Treated by Splenectomy and Further Observations on the Mechanism of Sickle-Cell Formation, *Am. J. M. Sc.* **175**:206-217, 1928.

31. Sydenstricker, V. P.: Sickle Cell Anemia, *South. M. J.* **17**:177-183, 1924.

32. Ching, R. E., and Diggs, L. W.: Splenectomy in Sickle Cell Anemia: Report of a Case with Necropsy in an Adult on Whom Splenectomy Was Attempted, *Arch. Int. Med.* **51**:100-111 (Jan.) 1933.

33. Washburn, R. E.: Peculiar Elongated and Sickle-Shaped Red Blood Corpuscles in a Case of Severe Anemia, *Virginia M. Semi-Monthly* **15**:490-493, 1910-1911.

34. Cook, J. E., and Meyer, J.: Severe Anemia with Remarkable Elongated and Sickle-Shaped Red Blood Cells and Chronic Leg Ulcer, *Arch. Int. Med.* **16**:644-651 (Oct.) 1915.

35. Mason, V. R.: Sickle Cell Anemia, *J. A. M. A.* **79**:1318-1320 (Oct. 14) 1922.

Steinfeld and Klauder ³⁶ reported the condition in a Negress 38 years old, but reports by dermatologists have been conspicuously few. Occasionally in recent years patients have been presented at meetings of local dermatologic societies: 1 by King ³⁷ (Philadelphia), 1 by Netherton ³⁸ (Cleveland), 1 by Schwartz ³⁹ (Cleveland), 2 sisters by Schwartz ⁴⁰ (Cleveland), 2 by Cummer and LaRocco ⁴¹ (Cleveland) and 1 by Krugh ⁴² (Pittsburgh).

REPORT OF CASES

The following cases have been observed in our service at St. Vincent Charity Hospital. The first will be described in detail, the others, more briefly.

CASE 1—W. M. G., a Negress aged 18,⁴³ was admitted to the medical division of the outpatient department on Dec. 22, 1933, complaining of "tired feeling" and pains in the joints. She had been seen in the surgical division at various times because of pains in the joints. The heart was enlarged, and there was a mitral systolic murmur. A diagnosis of compensated rheumatic heart disease was made. She reported at the dispensary at intervals, usually complaining of pains in the joints.

36 Steinfeld, E., and Klauder, J. V. Sickle-Cell Anemia, *M. Clin. North America* **10** 1561-1576, 1927. This description is the first one we have been able to find by dermatologists.

37 King, A. D. Sickle Cell Anemia, *Arch. Dermat. & Syph.* **33** 756-757 (April) 1936.

38 Netherton, E. W. Sickle Cell Anemia with Ulcer of the Leg, *Arch. Dermat. & Syph.* **34** 158-159 (July) 1936.

39 Schwartz, W. F. Sickle Cell Anemia Associated with Ulcers on the Legs, *Arch. Dermat. & Syph.* **37** 866-867 (May) 1938.

40 Schwartz, W. F. Ulcers of the Leg, Associated with Sickle Cell Anemia, in Sisters, *Arch. Dermat. & Syph.* **38** 1006-1007 (Dec.) 1938.

41 Cummer, C. L., and LaRocco, C. G. Two Cases of Chronic Ulcers of Legs in Patients with Sickle Cell Anemia, *Arch. Dermat. & Syph.* **39** 168-170 (Jan.) 1939, at the second presentation of 1 of these cases (Cummer, C. L., and LaRocco, C. G. Ulcers on the Legs in Sickle Cell Anemia, *ibid.* **40** 459-460 [Sept.] 1939) it was felt that the weight of evidence, especially the observation of a few giant cells and epithelioid cells in small tubercle formation, favored the diagnosis of tuberculosis. Although we feel that the argument is not entirely convincing, especially in view of the history of repeated complete healing followed by breaking down on numerous occasions, nevertheless there is enough room for reasonable doubt so that the diagnosis in this case should be revised.

42 Krugh, F. J. Sickle Cell Anemia. Ulcer on the Leg, *Arch. Dermat. & Syph.* **40** 656 (Oct.) 1939.

43 We presented this patient at a meeting of the Cleveland Dermatological Society on March 24, 1938.⁴¹ In discussion at this time attention was called to scars in the cervical region as suggesting the possibility of old tuberculosis. However, later questioning established the fact that the scars resulted from enlarged glands following osteomyelitis of the jaw from an infected tooth at the age of 12 years.

On March 13, 1936 she was seen in the surgical division with an ulcer on the leg. This had started as a pimple, which had been scratched. In spite of negative results of serodiagnostic tests, syphilis was considered, and intramuscular injections of bismuth subsalicylate were given. During this treatment there was temporary healing, followed by the breaking down of ulcers and the appearance of new ones. In November the Wassermann and Kline reactions were again negative, and numerous deep, irregularly shaped ulcers with arcuate configuration were found on the legs.

On Oct. 26, 1937 it was found that her second child, 2 years old, had been admitted to the University Hospitals of Cleveland about three months previously and had had a splenectomy for sickle cell anemia. The patient was referred to the wards of the hospital for study on March 7, 1938. The pupils were round, regular in outline and equal and reacted to light and in accommodation. The heart



Fig. 4 (case 1).—A, ulcers of the legs, showing bilateral and symmetric arrangement. B, large ulcer showing irregularly arcuate outline.

had a mitral murmur but was well compensated. The lungs were clear, and the abdomen showed no masses or tenderness. The spleen was not palpable. Ulcers were still present on both legs above the ankles. They were deep, irregular in outline, some several inches across, with sluggish bases.

The urine was normal. A blood count showed 4,100,000 red blood cells and 8,000 white blood cells per cubic millimeter and 70 per cent hemoglobin. The differential count showed polymorphonuclear neutrophils 67 per cent, small mononuclear leukocytes 24 per cent, large mononuclear leukocytes 6 per cent, transitional forms 4 per cent and eosinophils 2 per cent. Sick cells were found in wet preparations. The Wassermann and Kline reactions were negative. The icteric index was 3.5.

The following report was made by Dr. D. J. Rehbock after histologic examination of a section from the edge of one of the ulcers: "The section shows skin only at the margin of the tissue, and at the margin the skin has a relatively

normal appearance, there being only a small amount of lymphoid infiltration in the corium. The epithelial surface ends abruptly at the margin of the ulcer. The ulcer is covered with projecting masses of granulation tissue, beneath which is dense fibrous connective tissue heavily infiltrated with small mononuclear and polymorphonuclear cells. In several areas are multinucleated giant cells, but there are no typical tubercle formations. The underlying fat shows no changes. The pathologic diagnosis is chronic granulomatous inflammation of the skin with ulceration."

Roentgenologic examination showed that the skull, vertebrae and fibulas were normal, with no changes suggestive of sickle cell anemia.



Fig 5 (case 1) —Resulting scars. The ulcers were not healed until the end of two and a half years.

Local treatment of the ulcers consisted of mild antiseptic applications, such as boric acid ointment. Pills of ferrous carbonate U S P were given internally. After a duration of over two years improvement with partial healing was noted in April 1938. Healing was complete in August 1938, and there has been no recurrence to the time of writing. On Nov 7, 1938 examination of the blood showed 4,350,000 red blood cells and 10,400 white blood cells per cubic millimeter and 96 per cent hemoglobin. The differential count showed polymorphonuclear neutrophils 86 per cent, lymphocytes 12 per cent and eosinophils 2 per cent. A considerable proportion of sickle cells were found in wet preparations allowed to stand, although there were none in fresh preparations.

Summary.—In a Negress multiple ulcers of the legs appeared at the age of 21 years and required two and a half years for healing. Examinations of the blood showed sickle anemia, anemia of moderate degree and negative Kline and Wassermann reactions. Biopsy material from an ulcer showed chronic granulomatous inflammation of the skin with ulceration. Roentgenograms of the skull, vertebrae and fibulas were normal. Antisyphilitic treatment did not influence the course of the ulcers. Signs and symptoms included clear scleras, pains in the joints, malaise, cardiac enlargement and systolic precordial murmur. The spleen was not palpable. The patient's daughter had had a splenectomy for sickle cell anemia.

CASE 2.—D. J., a Negress, had multiple ulcers of the right leg which appeared in 1937 when she was 13 years old.⁴⁴ First there was a single lesion on the right shin. This had been scratched and became crusted. About a dozen other lesions appeared. The secondary lesions could have been interpreted as impetiginous, probably having spread from infection of the original lesion.

There was a history of attacks in which the patient had a greenish tint of the scleras. The Wassermann and Kline tests gave negative results. Reactions to

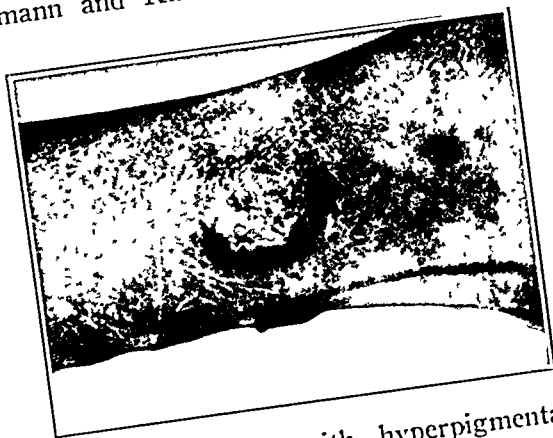


Fig. 6 (case 2).—Atrophic scar with hyperpigmentation of border.

tuberculin tests were negative. Biopsy material showed chronic ulcer with no specific changes. Signs and symptoms included cardiac enlargement, systolic precordial murmur and frequent attacks of pain in the head, joints and extremities. The spleen and liver were not enlarged.

Histologic examination showed that the epithelium over the tissue adjacent to the ulcer was normal. Near the edge of the ulcer the papillae were broader and extended down more deeply. Here the corium showed much new connective tissue and many capillaries and was infiltrated with lymphoid and plasma cells. The base of the ulcer was covered with granulation tissue in which sickle cells were rather numerous. There was no apparent increase in fibrous tissue beneath the ulcer. Giant cells were not seen. There were no changes in the walls of the blood vessels. Examinations of the blood at various times showed severe anemia, sickle anemia and other changes compatible with sickle cell anemia. Red blood cells ranged on three examinations from 2,200,000 to 2,340,000 per cubic millimeter; the leukocytes numbered 16,100 per cubic millimeter, and the hemoglobin amounted to 60 per cent. Sickled red blood cells were found on two occasions. The differential count of leukocytes showed polymorphonuclear neutrophils

44. Presented at a meeting of the Cleveland Dermatological Society on Sept. 30, 1937 by Dr. W. F. Schwartz.³⁹

cent. The resistance of the red cells to hypotonic solution of sodium chloride was increased. With the normal control hemolysis began with a 0.46 per cent solution and was complete with a 0.38 per cent solution, while the patient's blood showed beginning hemolysis with the 0.40 per cent solution and was not entirely complete even with the 0.28 per cent solution. The icteric index was 10. The sedimentation rate was 2 mm. in one hour, not corrected for anemia.

CASE 3—R. F., a Negress aged 15, had a circular, depressed, smooth scar on the leg. The history indicated that at the age of about 4 years there had been an ulcer on the leg, which had lasted months. Examination of the blood showed severe anemia, with observations compatible with sickle cell anemia. The signs and symptoms included green scleras, severe pains in the joints, weakness, cardiac enlargement, arrhythmia and a precordial cardiac murmur. The spleen was not enlarged.

The Wassermann and Kline reactions were positive, but healing had taken place without antisyphilitic treatment. Examination of the blood showed red blood cells, 2,610,000 per cubic millimeter, hemoglobin, 38 per cent, leukocytes, 12,800 per cubic millimeter, polymorphonuclear neutrophils, 68 per cent, small lymphocytes, 22 per cent, monocytes, 4 per cent, and transitional forms, 6 per cent. Crescent-shaped erythrocytes were found. The reticulocytes ranged from 0.4 to 0.6 per cent. The icteric index was 100 on one occasion and 26.5 five days later. In the test for resistance to hypotonic solution of sodium chloride, hemolysis began with the 0.34 per cent solution and was complete with the 0.28 per cent, while in tests of the normal control it began with 0.44 per cent and was complete with 0.40 per cent. The urine was normal, and there was no urobilin. Examination of the sternal marrow showed about the same percentage of sickled cells as in the blood. There was some increase in the number of normoblasts and erythroblasts. No change was noted in the white blood cells. The spinal fluid had a pressure equal to 110 mm. of water, it was clear, of normal color, showed 40 cells per cubic millimeter and gave a negative reaction to the gum mastic test. Roentgenologic examination of the skull and femur showed no abnormality but fibrosis of the lower third of the right lung.

CASE 4—L. C., a Negress aged 13,⁴⁵ had multiple punched-out ulcers on the legs which healed at the end of nine months. Healing would occur on one side with destruction on the other. The spleen was not palpable.

Examination of the blood showed 4,650,000 red blood cells per cubic millimeter, 80 per cent hemoglobin, 8,400 leukocytes per cubic millimeter and a color index of 0.86. The differential count showed polymorphonuclear neutrophils 52 per cent, lymphocytes 36 per cent, monocytes 4 per cent, eosinophils 4 per cent, mast cells none and transitional cells 4 per cent. Sick cells were looked for on nine occasions. On admission they constituted 15 to 20 per cent of the erythrocytes, but later only occasional ones were found. The reticulocytes ranged from 0.9 to 1 per cent on fourteen examinations. The Wassermann and Kline tests gave negative results, and there was no serologic response to a provocative injection of neoarsphenamine. The reaction to a tuberculin test was negative. Biopsy was not permitted.

⁴⁵ Presented at a meeting of the Cleveland Dermatological Society on April 28, 1938 by Dr. W. F. Schwartz.⁴⁰

CASE 5.—L. O. C., a Negress aged 14,⁴⁵ sister of the preceding patient, had multiple ulcers on the legs, which also required nine months for healing. These were punched out, with deep, sharp margins and gray, moist bases.

Examination of the blood showed: 4,950,000 red blood cells per cubic millimeter, 15,750 leukocytes per cubic millimeter and 90 per cent hemoglobin. A differential count showed: polymorphonuclear neutrophils 73 per cent, lymphocytes 15 per cent, monocytes 9 per cent, eosinophils 1 per cent and stab cells 2 per cent. The sickle cells ranged from 10 to 15 per cent on admission to 1 per cent or less on later examinations. The Wassermann reaction was negative on three occasions, and the Kline "diagnostic" test gave a negative reaction once and a 2 plus reaction twice. The reactions to tuberculin tests were negative. Biopsy was refused.

In our opinion the first 3 cases are definite instances of sickle cell anemia, the fourth probably so and the fifth possibly so, with a remission in the anemia at the time the blood was examined.

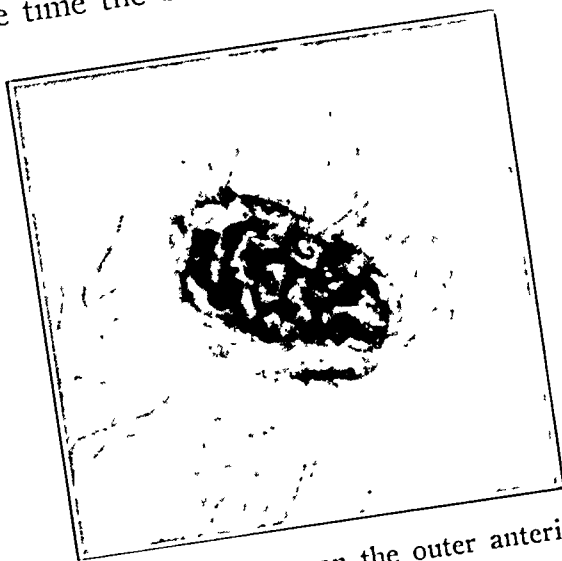


Fig. 7 (case 5).—One of the ulcers on the outer anterior surface of the right leg.

FREQUENCY OF OCCURRENCE OF ULCERS OF THE LEGS

After examining parallel series of Negroes with and without the trait, Diggs, Ahmann and Bibb⁸ stated that they did not feel that their statistical results supported the idea that the ulcers on the legs occurred more commonly in those with the trait than in normal persons. In regard to sickle cell anemia, on the other hand, Diggs and Ching² stated that chronic ulcers or scars of old ulcers are present in 3 of every 4 adults with the disease but are infrequent in young children. They gave the average age of patients at the time of appearance of the ulcers as 15 years.

Several series of cases are on record, and from them one may obtain statistics to aid in estimating the frequency of these ulcers. In Huck's⁹ series of 14 cases, there were ulcers on the legs in 2. Hein, McCalla and Thorne²⁵ collected 12 cases in the literature to 1927 and observed that

there were ulcers in the ankle region in 9 Corrigan and Schiller⁴⁶ observed and reported 8 cases, in which ulcers of the legs were noted in 1 and ulcers on the elbows in 2 Diggs, Pulliam and King²⁰ reported a series of 30 cases, in 9 of which there were ulcers on the legs Levy⁴⁷ described 9 cases and mentioned ulcers of the legs in 1 and numerous scars in another Anderson and Ware⁴⁸ collected from the literature 49 cases In the 28 in which mention was made ulcers of the legs were noted in 20 and were absent in 8 In studying this report one finds that in the group of patients showing ulcers, the age of the youngest was 8 years, all the others were 15 years of age or older, while those showing no ulcers ranged from ½ year to 13 years

DESCRIPTION OF ULCERS

In the available descriptions, one is impressed with the recurrence of the phrase "punched out" The ulcer may be single and unilateral, but multiple and bilateral ulcers are reported The most frequent location is in the neighborhood of the ankle, but any part of the leg may be involved The size ranges from that of a quarter or a half-dollar to much larger It is usually sharply margined, round or oval and may be shallow or deep The borders may be elevated and irregular The base usually shows granulation tissue and is occasionally suppurating or in some instances covered with dried serous or seropurulent crust The appearance may even be that of ecthyma The resulting scars are atrophic, glossy, smooth, depigmented and usually surrounded by a pigmented border or areola

In their course the ulcers are typically chronic but respond to palliative and simple measures, such as elevation of the leg with rest in bed and dressings of boric acid or zinc oxide ointment As Huck remarked, the disease itself has never been cured, but with treatment and rest the relapses are shortened and the remissions made longer Hard physical work is detrimental

HISTOLOGIC PICTURE

Huck's⁹ description is the earliest He observed that near the edge of the ulcer the papillae extended downward to an abnormal degree and that the connective tissue of the corium was increased above the normal amount The walls of the rather numerous blood vessels were not abnormal Throughout the tissues mononuclear wandering cells of the ordinary variety characteristic of chronic inflammation were scat-

46 Corrigan, J. C., and Schiller, I. W. Sickie Cell Anemia Report of Eight Cases, One with Necropsy, *New England J Med* **210** 410-417, 1934

47 Levy, J. Sicklema, *Ann Int Med* **3** 47-54, 1929

48 Anderson, W. W., and Ware, R. L. Sickie Cell Anemia, *Am J Dis Child* **44** 1055-1070 (Nov.) 1932

tered diffusely, although in most places the plasma and large mononuclear wandering cell types predominated over the small lymphoid type. Among these nonnuclear cells were a few neutrophilic polymorphonuclear leukocytes. In places the wandering cell infiltration was concentrated about small blood vessels and atrophic sweat glands, although many other blood vessels were entirely free from perivascular infiltration. The



Fig. 8 (case 2).—Hyperkeratosis and acanthosis in epithelium at the edge of an ulcer, with some broadening of papillary bodies and infiltration of corium ($\times 35$).

base of the ulcer was composed of granulation tissue possessing no characteristics suggestive of any specific causation. A few sickle-shaped red blood cells were seen.⁴⁹

49. To demonstrate sickle cells in the tissues, most investigators insist on the desirability of using a solution of formaldehyde as fixative rather than Zenker's solution.

Sydenstricker⁵⁰ described the section in 1 of his cases as showing extreme round cell infiltration of the skin and subcutaneous tissues adjacent to the ulcer, the base being filled with granulation tissue in which there was a moderate degree of polymorphonuclear infiltration. A



Fig 9 (case 2) —The edge of the ulcer, showing infiltration of corium with lymphoid and plasma cells to the left and the granulation tissue in the ulcer at the right ($\times 145$)

few giant cells were seen. In the biopsies reported here no change in the tissues was noted which might not be found in any chronic, non-specific ulcer.

⁵⁰ Sydenstricker, V. P. Further Observations on Sickle Cell Anemia, *J. A. M. A.* 83:12-17 (July 5) 1924.

DIFFERENTIAL DIAGNOSIS

With ulcers of the legs in a Negro patient, the differential diagnosis may be exceedingly difficult because of the lack of a characteristic clinical or pathologic picture.

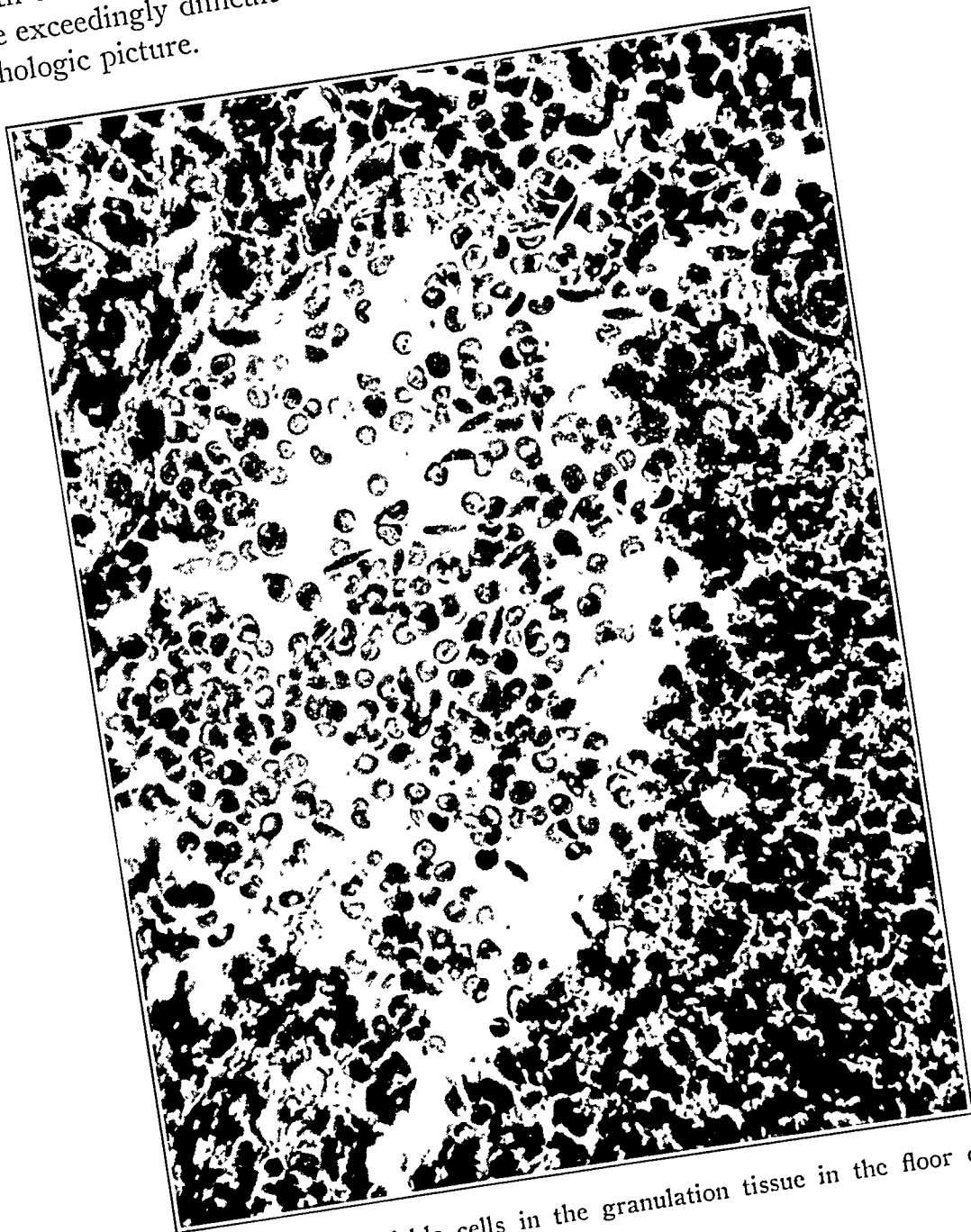


Fig. 10 (case 2).—Sickle cells in the granulation tissue in the floor of ulcer ($\times 605$).

Merely finding sickle cell anemia in a patient with ulcers of the legs does not of itself establish a causal relation. It is impossible to reply entirely on serologic tests to differentiate between ulcers due to sickle cell anemia and those due to syphilis, for the great frequency of positive results of serodiagnostic tests in Negroes is well recognized. Antisyphi-

litic treatment aids in establishing a diagnosis, since sickle cell ulcers show no response to it. Ecthyma seldom needs serious consideration. Erythema induratum rarely if ever occurs in males, its lesions by predilection are on the calf, while those of sickle cell anemia are usually over



Fig 11 (Dr C B Norris' case) —At the edge of an ulcer, with granulation tissue in the ulcer and in the corium, new connective tissue, many capillaries and infiltration with round cells and occasional polymorphonuclear leukocytes ($\times 140$)

the ankles or on the shins. Scrofuloderma occurs typically as an ulceration of the skin over tuberculous bones, joints or glands, with ragged, undermined edges and a base often covered with seropurulent exudate. With the tuberculous gumma, the history would indicate that the lesion started as a circumscribed nodular infiltration of the subcutaneous tissue,

gradually enlarging, with later involvement of the skin, and eventually breaking down to form an ulcer with a livid periphery and ragged, thin, undermined edges. A biopsy should be especially useful in establishing its tuberculous nature.

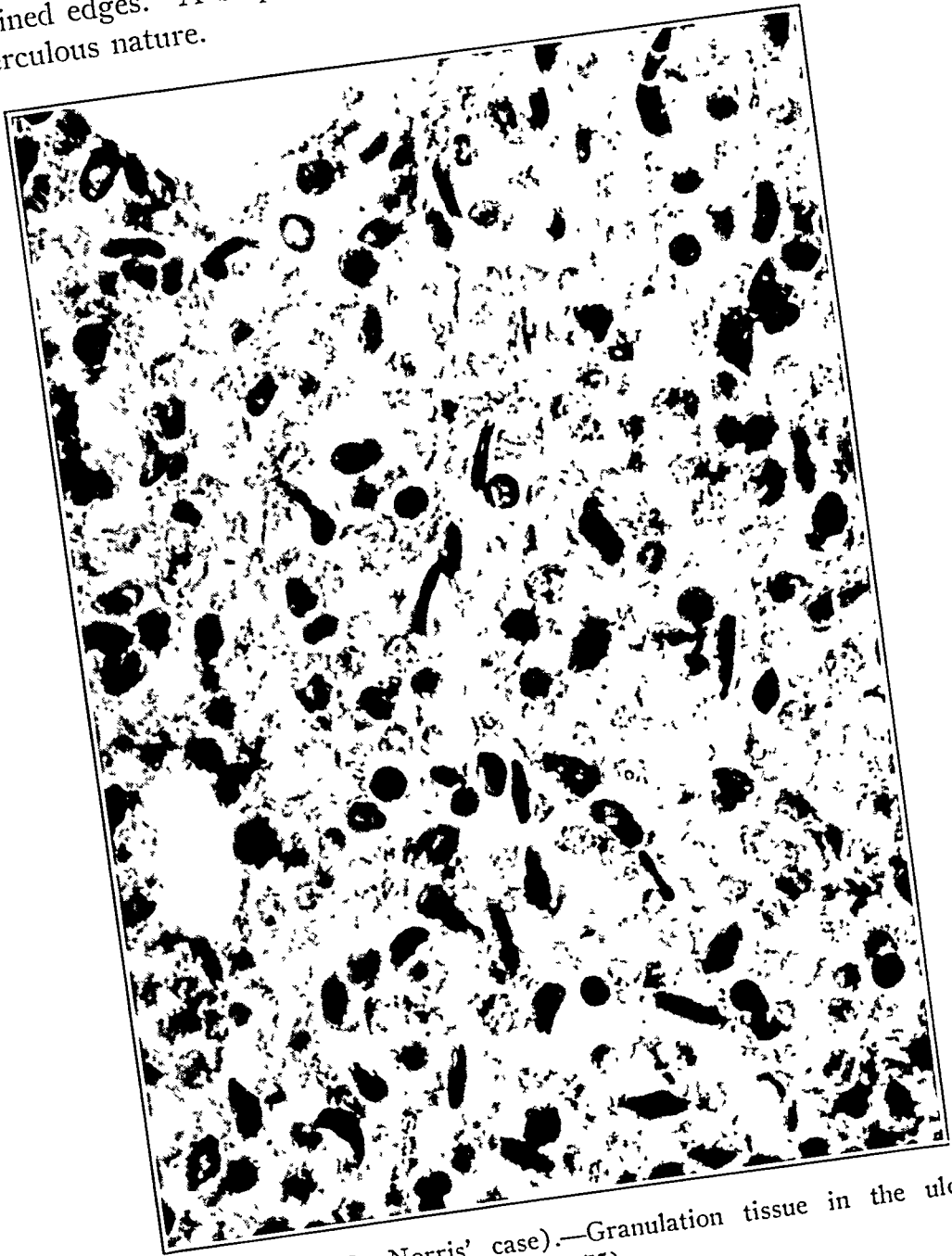


Fig. 12 (Dr. C. B. Norris' case).—Granulation tissue in the ulcer with elongated and crescentic erythrocytes ($\times 875$).

Traumatic ulcers in the acute stage are usually inflammatory and may present evidence of surrounding cellulitis. Although some of the sickle cell ulcers apparently start from minor trauma, the purely traumatic lesion heals comparatively quickly, while in a sufferer from sickle cell anemia, trauma initiates an ulcer characterized by destruction out of proportion to the original injury and by extremely slow healing. The

chronic ulcer of the leg so frequently seen in dispensary practice in association with varicose eczema and edema of the foot and leg is rarely encountered in adolescence and, in any event, should not cause diagnostic difficulty

ULCERS OF THE LEGS IN OTHER ANEMIAS

In considering ulcers of the legs in sickle cell anemia, the question of their occurrence in other forms of severe anemia naturally arises. Such ulcers have never been regarded as part of the clinical manifestations of pernicious anemia, although there is a recent report by Lasch⁵¹ of a 44 year old man suffering from pernicious anemia who showed symmetric, deep, palm-sized ulcers on both legs above the ankle joints. These had not healed under treatment with salves but did with liver therapy. In an article by Chevallier⁵² on dermatoses of the anemias there is no reference to ulcers on the legs. In a recent publication by Murphy⁵³ such ulcers are not mentioned as occurring in chlorosis.

However, with congenital hemolytic jaundice the case is different. Taylor⁵⁴ recently recounted the case of a woman 20 years old with congenital hemolytic jaundice who had an ulcer of twelve months' duration which healed promptly after splenectomy and had remained healed when last seen nine months after surgical treatment. He found reports of 17 similar cases in the literature. Since then McGovern⁵⁵ has presented at the Montreal meeting of the American Dermatological Association a white man, 23 years old, with hemolytic jaundice who had been under observation for two years for indolent multiple ulcers of both legs. Biopsy showed chronic ulcer with fibrosis at the base and recent extensive hemorrhage. Murphy⁵³ likewise referred to the finding of ulcers on the legs in familial hemolytic jaundice.

COMMENT

An attempt to explain the causation of ulcers of the legs in sickle cell anemia might well lead into theoretic speculation. At hand are the following facts:

1. Such ulcers occur in a definite proportion of persons suffering from sickle cell anemia and in a lower proportion of those with the sickle cell trait only.

51 Lasch, F. Ueber Beingeschwüre bei perniziöser Anämie, *Deutsche med Wchnschr* **65** 377-378, 1939.

52 Chevallier, P. Die Dermatosen der Anaemie, *Med Welt* **10** 120-122, 1936.

53 Murphy, W. P. *Anemia in Practice. Pernicious Anemia*, Philadelphia, W. B. Saunders Company, 1939.

54 Taylor, E. S. Chronic Ulcer of the Leg Associated with Congenital Hemolytic Jaundice, *J. A. M. A.* **112** 1574-1576 (April 22) 1939.

55 McGovern, J. J. Hemolytic Jaundice with Ulceration of the Skin, *Arch Dermat & Syph* **41** 408-409 (Feb) 1940.

2. They must be rare in pernicious anemia and chlorosis, at least sufficiently so that they are not generally referred to in articles on these disorders, but they are encountered in congenital hemolytic jaundice. It is possible that they occur more frequently than is recognized now.

3. Sickle cell anemia and congenital hemolytic jaundice present different hematologic pictures. In sickle cell anemia the erythrocytes frequently show elongated forms while in congenital hemolytic jaundice they are spherocytic and microcytic. In the former the fragility of the red blood cells as determined by tests with hypotonic solution of sodium chloride is decreased whereas in the latter the reverse is true. However, Murphy⁵³ has advanced the opinion that sickle cell anemia may be considered as the typical manifestation of familial hemolytic anemia in the Negro. It is his opinion that in place of the spherical erythrocytes characteristic of congenital hemolytic jaundice, sickle cells appear in the Negro, possibly because of some difference in the structure of the erythrocytes in Negroes as opposed to those in white persons.

4. In many case reports it is evident that the ulcers in sickle cell anemia seem to have been induced, or at least preceded, by infection or trauma. The size and duration of the ulcers are out of all proportion to the severity of the original infection or trauma.

5. The ulcers in sickle cell anemia show no specific histologic picture to distinguish them from other chronic ulcers.

With these facts at hand, the following theories may be advanced and evaluated. The first is that the ulcers have been produced by injury or infection and have become chronic simply because of associated malnutrition or the lowered vitality of anemic tissue. Against this is the present apparent lack of evidence that similar lesions occur in other severe anemias, notably chlorosis, a condition which affects adolescent girls in the same age period as those with sickle cell anemia in whom ulcers of the legs most frequently develop. That they are coincidental only is not plausible, because they occur more often in those with sickle cell anemia than in those with the nonsymptomatic trait. An explanation of the capillaries by the greatly elongated erythrocytes, would be an attractive one but has no histologic evidence and would not explain similar ulcers in chronic hemolytic jaundice, in which thromboses are not a part of the pathologic process and in which the erythrocytes are not elongated but spherocytic.

Ultimate decision must await further and more complete clinical investigation. As Senear⁵⁶ remarked, the opportunity of studying a most interesting new condition in dermatology will be provided if anemia is considered as a possible explanation for old chronic ulcers on the legs, especially in young persons.

56. Senear, F. E., in discussion on McGovern.⁵⁵

SUMMARY

The sickle cell trait is limited almost exclusively to persons of the Negro race, occurring in about 8 per cent. It is familial and apparently hereditary. There is no preference for sex and no difference in percentage incidence in different sections of the country. Anemia, which is found only in some of those who show sickle cells in the peripheral blood, may be accompanied by some or all of a group of signs and symptoms, which includes ulcers on the legs.

Histories of illustrative cases in which ulcers occurred on the legs have been recounted. It is impossible to state definitely the frequency of occurrence of ulcers or scars of ulcers, because of the insufficiency of statistical data, but in the largest series of collected cases, numbering 28, ulcers or scars were noted in 20.

The ulcers are usually punched out in appearance, may be single or multiple and unilateral or bilateral and are most frequently in the neighborhood of the ankle. The course is extremely chronic. Simple local applications seem the most effective treatment. No treatment is known for the underlying anemia.

The histologic picture is that of chronic granulomatous ulcer.

Diagnosis rests on the finding of a hemolytic type of anemia with sickle cells in the peripheral blood, chronicity, the absence of specific architecture in the histologic examination of biopsy material and the failure to respond to antisyphilitic treatment when the results of sero-diagnostic tests for syphilis are positive.

The mechanism of the causation of the ulcers on the legs is an open question. Undeniably many seem to have been initiated by minor infection or trauma. That they are also seen in congenital hemolytic jaundice is of interest and suggests that a common causative factor may be found.

In dermatologic practice anemia should be considered as a possible explanation for old chronic ulcers on the legs, especially in younger persons.

Dr Harold N. Cole and Dr J. R. Driver gave permission to refer to the histories of cases 2, 4 and 5, observed in their service at the Cleveland City Hospital as well as in our own service. Dr Gerard DeOreo assisted in collecting data and photographs. Prof. Howard T. Karsner made photomicrographs at the Institute of Pathology of Western Reserve University. Dr Louis W. Ladd, Jr. and Dr M. I. Sparks made the hematologic studies in 2 cases. Dr Fred C. Oldenburg gave permission to report cases observed in the medical service of St. Vincent Charity Hospital.

The photomicrographs in figures 11 and 12 are from the case reported by Netherton³⁸. Dr Claude B. Norris, who saw the patient originally, procured the slide for us.

1010 Hanna Building, 1422 Euclid Avenue
669 Rose Building, 20 East Ninth Street

ABSTRACT OF DISCUSSION

DR. E. W. NETHERTON, Cleveland: This excellent presentation by Dr. Cumber and Dr. LaRocco is a timely one. Although in the first case, which was reported by Herrick, there were ulcers of the legs, there is only one article in the dermatologic literature in this country which places any emphasis whatever on this entity.

It is well known that sickle cell anemia is almost always observed in Negroes, although there have been a few apparently bona fide cases reported in white persons. In some of those cases, however, it has not been possible to rule out with certainty the possibility of Negro blood. The sickling trait has a higher incidence among Negroes. Although 8 per cent of the Negroes show this trait, a much smaller per cent show the anemia. Only in a case in which the anemia develops is one apt to see this particular type of ulceration. The spleen in sickle cell anemia is invariably large early in the disease, while late in the disease it is apt to be small, often impossible to be detected when splenectomy is attempted in the treatment of this disease. Repeated infarcts and subsequent sclerosis lead to atrophy of the spleen. I mention that because it may at least be of some theoretic importance regarding the pathogenesis of these ulcers.

Dr. Cumber mentioned that there is no explanation for the mechanism producing these ulcers, but all the histologic studies have been made on late lesions, in which the early initial change has been cast off as the ulcer formed. As he has emphasized, the theory of trauma plus secondary infection will not explain the mechanism. Formation of ulcers in this way obviously occurs in all anemias. However, only in this particular anemia is this type of ulcer found. Therefore, I believe that if some one could obtain the tissue from a very early lesion, which is not easily done, and make serial sections, he might find certain vascular changes, such as thrombi, in the early tissue changes similar to those frequently occurring in the spleen.

I think that if more careful search is made for cases of this kind, it will be found that they are more common than was believed.

DR. MARTIN T. VAN STUDDIFORD, New Orleans: Dr. Cumber, in his paper, has introduced the discussion of a condition which is known to exist but which is seldom seen. When ulcers of the legs are shown to medical students, they proffer a diagnosis of "sickle cell anemia ulcer," whereas the condition is usually a syphilitic or a varicose ulcer.

Of the many cases of sickle cell anemia observed in St. Vincent Charity Hospital over twenty years, I have just lately had a patient, a Negro boy 4 years old, who has ulcers over traumatic areas from his waist to his ankles. He has a total erythrocyte count of 200,000 per cubic millimeter and has received five transfusions. A doughy "pot belly" is developing, and he is becoming emaciated over the chest and shoulders.

DR. CLYDE L. CUMMER, Cleveland: Haden and Evans studied the literature, carefully analyzed all the cases presumably reported in white persons and concluded that after any possibility of a trace of Negro blood had been ruled out—of course, that is difficult to do—there were 8 authentic examples of the condition in white persons, practically all in Italians or in persons of Mediterranean stock.

It is interesting, with that in mind, that there is a similar type of anemia, so-called Cooley's erythroblastic anemia or the Mediterranean anemia, which occurs in persons of Mediterranean stock (Wintrobe, M. M.; Matthews, E.; Pollack, R., and Dobyns, B. M.: Familial Hemopoietic Disorder in Italian Adolescents and Adults Resembling Mediterranean Disease [Thalassemia], *J. A. M. A.* **114**:1530 [April 20] 1940).

MASSIVE DESTRUCTION OF THE FACE

CHARLES C DENNIE, M D

Professor of Dermatology

THOMAS R HAMILTON, M D

Assistant in Pathology

AND

HENRY F QUINN, M D

Resident in Dermatology

KANSAS CITY, KAN

Massive destruction of the face is rather a rare condition. A diversity of etiologic factors have been given credit for its production. Among the principal causes of the condition are syphilis, frambesia, extensive rodent ulcer, tuberculosis, leishmaniasis (American), leprosy and gangosa (probably a tertiary form of frambesia).

The two main possibilities to be considered in the case to be reported are syphilis and American leishmaniasis. In America it is hard to prove that a case is one of leishmaniasis. It may have all of the typical findings, and yet the etiologic factor cannot be demonstrated. We observed such a case in the Kansas City General Hospital for nine months, in consultation with Dr. Paul F. Stookey.

The patient was a Central American who came to the hospital because of a perforation in the septum of his nose and a fissure at the junction of the left nostril and the lip. All serologic reactions were negative, and there was no history of syphilis. The disease progressed until the patient before death had lost not only his nose but his upper jaw, malar bones, eyes and lower jaw. Histologic examination of the tissues showed no leishmanias. Inoculation of diseased material into guinea pigs gave negative results. A section of the tissue was sent to Montenegro in Rio de Janeiro, Brazil. He was unable to demonstrate such bodies. A complete autopsy revealed no significant changes and no confirmatory evidence of leishmania infection.

According to Wilson and others, American leishmaniasis does not attack the viscera or the lungs. On the other hand, physicians of South America, where the disease is prevalent, in personal conversation told one of us (C. C. D.) that in American leishmaniasis the viscera are often involved.

From the University of Kansas School of Medicine

Read at the Sixty-Third Annual Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo.

REPORT OF A CASE

History.—A man aged 38, a native Kansan, who had never been outside of the United States, was admitted to the hospital in February 1938, complaining of a discharge from his nose. There was an indefinite history of syphilis nine years before his entry into the hospital. He stated that a white spot had developed in the roof of his mouth, which disappeared when he was given several injections in the arm and in the hip.

When the patient was first admitted to the hospital, a diagnosis was made of chronic ethmoid sinusitis and infection of both antrums. The treatment at that time consisted of the exploration of the left frontal sinus and right antrotomy. The serologic reactions for syphilis were negative.

He was admitted again on July 27, 1938, at which time a diagnosis was made of perforation of the septum due to syphilis. He remained only a few days and was discharged from the hospital. He was readmitted in November, at which time we saw him.

Physical Examination.—The patient was rather poorly nourished but fairly well developed and not acutely ill and had a red, swollen, shiny nose, with a rounded tumor on each side involving the tear duct (bilateral dacrocystitis). There was an offensive discharge from the nose. The nasal septum showed a perforation more than 2 cm. in diameter. The entire nose was tender and greatly enlarged, so that it drifted down toward the corner of the mouth. There were no abnormalities in the throat, but an examination of the neck showed some enlargement of the lymph nodes at the angle of the jaw. The chest was normal, and no abnormalities of the heart were discovered. An examination of the abdomen revealed no palpable organs or masses. The reflexes were physiologic. The extremities were normal. The nose, which at first showed no ulceration on the outside, became necrotic on the left side. It became plastic and drifted down over the upper lip. The process continued until the nose was entirely destroyed. Accompanying this destruction, the walls of the sinuses disappeared, the upper jaw disappeared, except for a thin strip of bone, the sphenoid sinus was exposed, and both eyes became involved, with final total blindness. A huge opening was made in the face, of such magnitude that the convulsive action of the esophagus could be clearly seen.

Laboratory Tests.—Serologic reactions for syphilis of both the blood and the cerebrospinal fluid were negative. There were moderate anemia and a moderate increase in leukocytes. A dark field examination of the material draining from the nose showed the presence of numerous spirochetes, which were of two types: the large, coarse spirals of Vincent, together with fusiform bacilli, and smaller, motile spirochetes morphologically identical with *Spirochaeta pallida*. It was considered at this time that the patient had syphilis but was suffering from a negative phase of it; in other words, his immunologic forces were so low that he had no resistance to his syphilis. He was given potassium iodide and intramuscular injections of a bismuth compound, with no benefit. Hyperpyrexia by means of hot baths was then instituted. After administering ten baths, in which the temperature was raised to 105 F., without improvement, the treatment was changed to the intravenous administration of typhoid bacterin. After a large number of successful elevations in temperature, this method was discontinued as the disease was progressing rapidly. By this time he had lost the left side of his nose and had so much necrotic material in his face that a surgical operation was performed to remove the material. Several doses of mapharsen were given,

without result. The two types of spirochetes could still be demonstrated in the secretions from his nose. He died on Aug 18, 1939.

Autopsy—The anatomic diagnoses were ulcerating phagedenic granuloma of the face and frontal portions of the skull, extensive necrotizing cellulitis of the face and head, chronic abscess of the brain (right frontal lobe), localized chronic pachymeningitis, bilateral confluent bronchopneumonia with early abscess formation (right lung), acute fibrinous pleurisy, acute dilatation of the heart, parenchymatous degeneration of the liver and kidney, and acute and chronic splentitis.

Histologic Examination—Sections of material from several places in the active lesions about the face were made. The stratified squamous epithelium was irregularly thickened and ulcerated at a number of points. In some areas the superficial squamous cells showed extensive vacuolation. The underlying hyaline fibrous



Fig 1—Massive destruction of the face

connective tissue showed a few, diffusely scattered mononuclear leukocytes. In other places there was a distinct mononuclear perivascular infiltration, with an increase in blood vessels to such an extent that it had the appearance of an angioma. There were no carcinomatous cells demonstrated. Sections taken from the diseased areas of the face were impregnated by the Levaditi method, and numerous spirochetes of two varieties were demonstrated: the large, coarse spirals belonging to the Vincent group and the smaller, sharply turned spirals, morphologically similar to *S. pallidae*. On numerous occasions these same organisms had been demonstrated by dark field illumination and by Fontana's stain. These organisms did not disappear on the administration of mapharsen. They were present in the tissue until the patient's death.

Liver—The liver was lobulated. The capsule was irregularly thickened. A few clumps of red blood cells were adherent to the surface. A few patches of liver cells were seen showing rather marked vacuolation. In other areas the liver cells were irregularly swollen and the sinusoids were compressed. There was considerable congestion, particularly in the central zone throughout the organ.

The portal spaces showed moderate mononuclear infiltration. Some of the blood vessels contained masses of agglutinated red cells, together with fibrin and a few leukocytes.

Spleen: The capsule of the spleen was not thickened. The trabeculae were not unduly prominent. The malpighian bodies were rather numerous and well defined. The sinusoids throughout the pulp were prominent, and there was diffuse

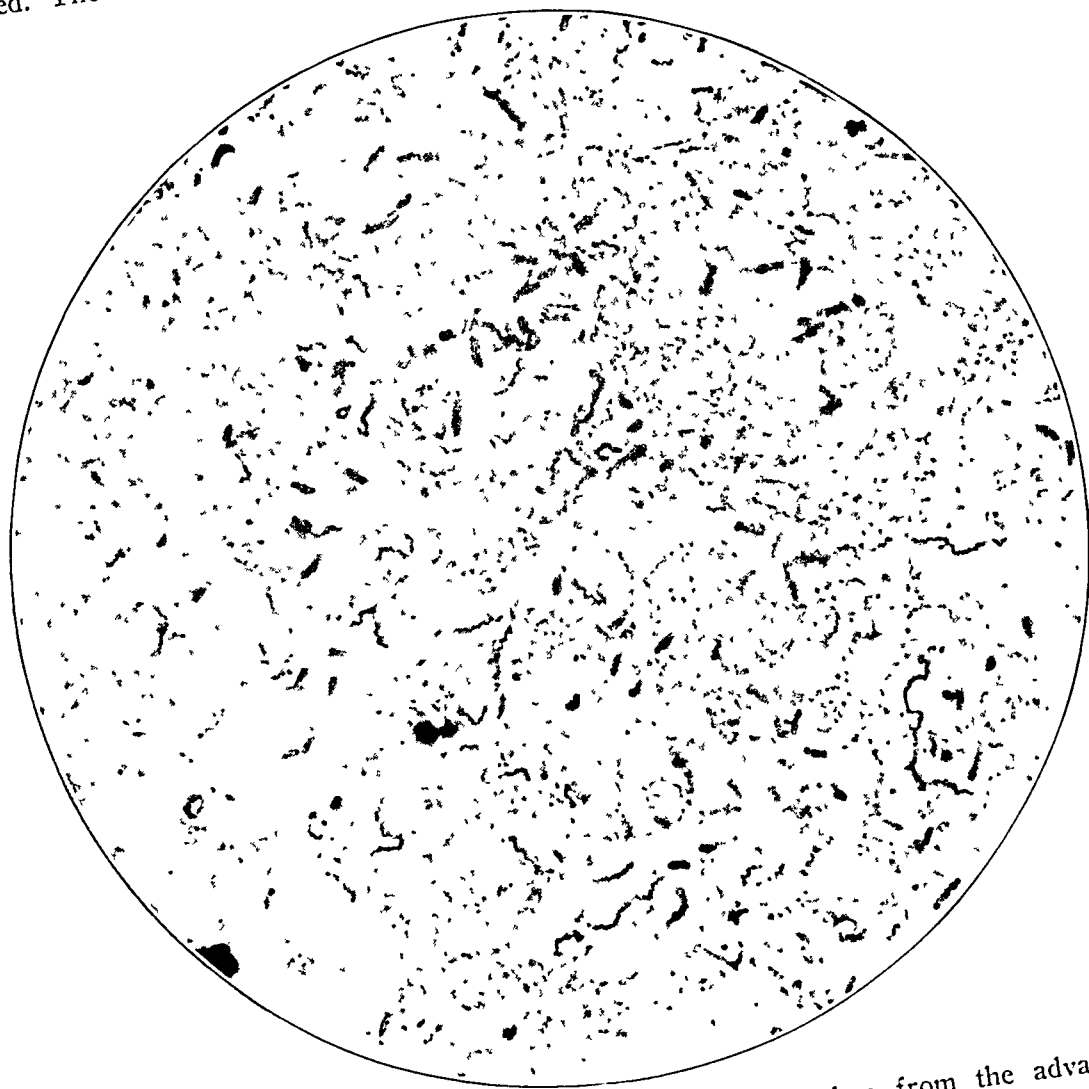


Fig. 2.—Photomicrograph of a section of tissue taken from the advancing border of a gigantic ulcer of the face, showing *S. microdentium* and some of the larger spirals belonging to the Vincent group.

fibrosis. Polymorphonuclear leukocytes were scattered throughout the pulp, and the sinusoids were considerably congested.

Brain: The thickened dura was adherent to the arachnoid on the right anterior lobe of the cerebral hemisphere. This area was contiguous to the diseased portion of the skull. Marked pachymeningitis was present. Beyond this was a small abscess, extending 1.5 cm. into the brain substance. The abscess was surrounded by a dense yellowish gray fibrous material. The histologic picture was that of chronic granuloma.

Animal Experimentation—Several months before the patient died, material was removed from the face and injected into the testes of two rabbits. At the end of three days a distinct chancre developed in one rabbit, which cleared up in about ten days. In the other rabbit a chancre developed in three weeks, from which both types of spirochetes, already described, were recovered on dark field illumination, by Fontana's stain and by Levaditi's impregnation method. In the rabbit in which the successful inoculation was secured a sloughing, gangrenous ulcer developed, which extended to and through the inguinal region and produced the rabbit's death. An inoculation from this rabbit to a tandem rabbit produced a chancre-like lesion, but unfortunately the rabbit died before we were able to complete our work.

COMMENT

We were unable to demonstrate Leishmanias in any of the tissues, although a more complete examination is yet to be made.

We do not believe that the spirochetes that were demonstrated were *S. pallida*, in spite of the fact that they were morphologically identical with it. The coarse spirals undoubtedly belong to the Vincent group. We are of the opinion that the small spirals belong to the microdentium family. *Spirochaeta microdentium* is a normal inhabitant of the mouth. It is considered to be nonpathogenic, yet we have encountered cases of partial destruction of the jaw in which the only organisms found were of this species. We believe that these organisms are capable of becoming pathogenic in persons who are in an anergic state. The massive destruction of the face can be produced by these spirochetes, similar to the condition produced in the cheeks of children known as noma or cancrum oris. One of us (C C D) demonstrated such spirochetes in the gangrenous tissue of an infant's cheek. The primary seat of attack was the nasal septum. The tear ducts were secondarily involved.

SUMMARY

We present a case in which we believe *Spirochaeta microdentium* was responsible for the massive destruction of the face, although it is hard to prove this assertion. We have not eliminated the possibility of American leishmaniasis.

1524 Professional Building

ABSTRACT OF DISCUSSION

DR A BENSON CANNON, New York. In the past several years a number of cases similar to the one presented here have been observed. In almost every instance the diagnosis was one of a variety of conditions: syphilis, tuberculosis, carcinoma or noma. The destructive process usually appeared after an operation, such as an appendectomy, or after ineffective treatment of a local injury or of a disease, such as syphilis or an abscess.

I recall that a number of years ago I was called in consultation with the late Dr. George E. Brewer on a case of massive destruction of the abdominal wall, which had occurred after the removal of an apparently innocent appendix.

Around the stitch wound there appeared ulcerations, which spread rapidly over the skin and soft parts, extending down to the fascia and involving the entire abdominal wall. The patient died, as did 3 or 4 others with similar conditions whom I have seen since.

In 1926 Dr. Frank Meleney, who made extensive bacteriologic investigations in several cases of the same condition, reported with Dr. Brewer (*Ann Surg.* 84:438 [Sept.] 1926) that they had been able to isolate from the wounds of these patients an anaerobic, microaerophilic, nonhemolytic strain of *Streptococcus* and also a hemolytic strain of *Staphylococcus aureus*, and that they considered the ulcerations to be due to the symbiotic action of the two micro-organisms. Brewer and Meleney treated the wounds with hydrogen peroxide and then packed them with gauze wet with solution of formaldehyde for two days, after which they applied the Carrel-Dakin treatment (with dilute solution of sodium hypochlorite). The improvement was immediate and progressive, the wounds healing rapidly and the patients all recovering within a few weeks or months.

Recently at the Vanderbilt Clinic I encountered a similar case in which after surgical removal of an axillary gland the entire axilla and the greater part of the skin and subcutaneous tissue of the chest wall on the side operated on sloughed away. This patient was presented at a local meeting of dermatologists, who were about equally divided in their opinion as to whether the condition was tuberculosis or syphilis. After about eleven months of treatment for the two diseases the patient was admitted to the Presbyterian Hospital, where he was studied and treated by Dr. Meleney in the manner used by Brewer and Meleney in the cases to which I referred, and was discharged as cured a few months later.

At a recent meeting of the New York Academy of Medicine a syphilitic patient from the Vanderbilt Clinic was shown in whom the nose as well as the adjacent portions of the cheek and lip had sloughed away, in spite of the fact that he was receiving active antisyphilitic therapy (old arsphenamine, a bismuth preparation and iodides). The spreading of the ulcerative process was checked only after vigorous local antiseptic treatment of the type advocated by Brewer and Meleney.

I could enumerate a number of additional interesting cases of similar nature in which the condition has responded to this treatment when all other remedies had failed.

I do not believe that the dermatologists in general have been as quick to recognize the value of the antiseptic method of treatment as have the surgeons, by whom it was so carefully and thoroughly worked out in the first place. I feel strongly that in cases of destructive processes of the type presented here one should not overlook the therapeutic possibilities inherent in the Carrel-Dakin method of treatment.

DR. CHARLES C. DENNIE, Kansas City, Kan.: I neglected to state that there were certain areas in the face in which there were large collections of small blood vessels. The pathologist was inclined to make a diagnosis of angioma.

Aseptic dressings were used, and the dead tissue was removed wherever possible.

I believe, in agreement with Dr. Wile, that the process in this case was one of endarteritis, continuous, with necrosis, due to *S. microdentium*.

ACETYLGLYCARSENO BENZENE IN TREATMENT OF SYPHILIS

PRELIMINARY REPORT

WILLIAM H GUY, M D

BERNHARD A GOLDMANN, M D

GEORGE P GANNON, M D

AND

JACOB SLONE, M D

PITTSBURGH

Since Ehrlich's discovery of arsphenamine did not accomplish the desired millennium in the treatment of syphilis, scientific workers have been constantly seeking to improve the known methods of attack on this disease. These endeavors have been directed toward better management of the courses of treatment, modifications in the dosage of drugs, variations in the methods of administration and the addition of new chemical compounds. During the past two years we have conducted a clinical study with a new drug in 84 cases of various types of syphilis. An arsenical compound having the common name of acetylglycarsenobenzene was administered intramuscularly, together with an oil-soluble bismuth compound and insoluble mercury. The patients were a selected group who had not received previous antisyphilitic treatment. In each instance the diagnosis of syphilis was supported by a dark field examination or by a serologic test.

CHEMISTRY

Acetylglycarsenobenzene is chemically 3,4'-diacetylamino-4-hydroxy-arsenobenzene 2'-sodium glycolate. The molecular weight is 530. The arsenic content is 28.3 per cent. The formula may be expressed as $C_{18}H_{17}O_6N_2As_2Na$ and graphically as



From the Department of Dermatology and Syphilology, University of Pittsburgh School of Medicine

Read before the Section on Dermatology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940

GUY ET AL.—SYPHILIS

The drug was available in a sterile aqueous solution with 10 per cent glycerin plus 0.005 Gm. per cubic centimeter of ascorbic acid. Each cubic centimeter of the sterile solution contains 0.07 Gm. of the active constituent; in arsenic content (0.02 Gm.) this is approximately equivalent to 0.1 Gm. of neoarsphenamine. The solution in ampules is orange-yellow and neutral or faintly acid in reaction.

*Local Tolerance.*¹—The local effects of acetylglycarsenobenzene were studied after subcutaneous as well as intramuscular injections of 0.1 to 0.2 cc. into adult albino rats. Groups of 12 animals were killed one, three and six days after treatment, and the sites of injection were examined. The subcutaneous and intramuscular injections produced a slight edema and congestion at the twenty-fourth hour, but little or no remarkable effect was demonstrable either three or six days after injection. Intramuscular (gluteal) injections into the upper and outer third of the buttock of man were tolerated satisfactorily, with no symptoms other than those of pressure, for from three to twenty minutes after injection.

Systemic Tolerance.—Studies of the toxicity of acetylglycarsenobenzene were made by intravenous injection into the albino rat, according to specifications of the National Institute of Health. These indicated satisfactory tolerance of not less than 400 mg. per kilogram of body weight given intravenously. When the drug was given intramuscularly the corresponding tolerated dose was 500 mg. per kilogram of body weight. (The National Institute of Health standard of tolerance for neoarsphenamine injected intravenously in the rat is 240 mg. per kilogram.)

Therapeutic Index.—In experimental infection with *Trypanosoma equiperdum* in rats, the curative dose of acetylglycarsenobenzene was found to be 12 mg. per kilogram intravenously. The therapeutic index (or maximum tolerated dose divided by the curative dose) thus exceeds 30.

Excretion.—The excretion curve was studied in a series of 6 adult rats after the intramuscular injection of acetylglycarsenobenzene in a dose of 50 mg. (14.28 mg. of arsenic) per kilogram of body weight. The peak of urinary excretion was observed during the first twenty-four hours; the values decreased during the following six to eight days, but a trace was still being excreted on the thirtieth day. The peak of fecal excretion occurred on the third to fourth day, and only traces were present on the eleventh day. A total of 58.5 per cent of the administered dose was recovered during the twenty-one days of study, which had

1. Data on local tolerance, systemic tolerance, therapeutic index and excretion are based on experiments by O. W. Barlow, Ph.D., M.D., Director of Pharmacologic and Biologic Research, Winthrop Chemical Co., Inc.

increased to 60 per cent on the thirtieth day. For purposes of comparison, neoarsphenamine was injected intravenously in a series of 6 cats in a dose of 50 mg per kilogram of body weight. During the succeeding twenty-one days, 38.75 per cent of the administered dose was recovered from the urine and feces. The data indicate that the ratio of the urinary excretion to the fecal excretion of arsenic after intramuscular injection of acetylglycarsenobenzene exceeds that after intravenous injections of neoarsphenamine.

In dogs the peak of urinary excretion of arsenic following the intramuscular injection of 350 mg per kilogram of body weight of acetylglycarsenobenzene occurred on the second day. A total of 67 per cent of the administered dose was recovered from the urine and feces during twenty-one days.

In human beings the excretion of arsenic following the injection of arsphenamine in terms of the administered dose was from 0.9 to 2.5 per cent on the first day, from 3 to 8.8 per cent in three days and from 4.9 to 13.5 per cent in fourteen days.

Weiss and Raiziss² reported 2.2 per cent excretion of neoarsphenamine during the first twenty-four hours. Corresponding observations on 3 normal men who received at three day intervals two intramuscular injections of 175 mg each of acetylglycarsenobenzene gave the following excretion data: 21.5 per cent on the first day, 31.7 per cent in three days and 34.8 per cent in fourteen days.

REVIEW OF THE LITERATURE

A review of the literature discloses a number of European publications on the clinical use of acetylglycarsenobenzene (under the trade name "solusalvasan") since 1932. These publications in the main attribute to the drug a clinical efficacy comparable to that of other arsenicals. Unfortunately, a number of these earlier reports are based on relatively short clinical studies which do not permit accurate deductions. We believe that at least two years' study is necessary for a preliminary evaluation of any antisyphilitic drug.

In 1932 Bezecky³ presented the first publication on the clinical investigation of acetylglycarsenobenzene. From his experiences he concluded that the drug is an effective antisyphilitic preparation and that intramuscular injections in amount large enough to produce a therapeutic action could be administered without pain.

2 Weiss, C., and Raiziss, G. W. Elimination of Arsenic in Urine of Syphilitic Patients After Intravenous Injection of Arsenic, *Arch Int Med* **30** 85 (July) 1922.

3 Bezecky, R. *Dermat Wchnsch* **94** 611 (April 30) 1932.

Ensbruner⁴ summarized his study by stating that in respect to spirocheticidal properties, influence on syphilitic lesions and tolerance the drug is an effective preparation.

Sainz de Aja and Forns Contera⁵ found the drug to be superior to other arsenical preparations administered intramuscularly and to be well tolerated.

Van Putte⁶ remarked that acetylglucarsenobenzene is better tolerated than neoarsphenamine.

Wendt⁷ concluded after a three years' study in the treatment of early syphilis that this drug is the drug of choice in cases in which intravenous injections are to be avoided. In a rather extensive series he observed no side effects.

Scherber⁸ recommended its use in patients with "poor veins" and in those who react to injections of neoarsphenamine, and it was his opinion that it can replace the latter.

A number of side effects have been reported abroad, but our experience indicates that these reactions were often due to improper dosage, either an excess of drug or inordinate frequency of administration.

Fasal and Konrad⁹ reported fatal complications following the intramuscular injection of the drug in 2 patients.

Grieco¹⁰ reported a case of vesicular edematous erythroderma. Wendlberger and Hrad¹¹ stated that the sole advantage of the drug would seem to be the fact that it is available in stable form, but owing to the complications of dermatitis, they recommended its use intravenously whenever feasible.

Harrison¹² considered the therapeutic action to be weaker than that of neoarsphenamine and the toxicity greater, particularly with respect to dermatitis, and did not advocate its use in the treatment of syphilis.

CLINICAL STUDY

Our investigation of acetylglucarsenobenzene has extended from March 1938 to April 1940. During this time 84 patients were given twenty-one hundred intramuscular injections of the drug. In addition

4. Ensbruner, G.: *Dermat. Ztschr.* **65**:28 (Nov.) 1932.
5. Sainz de Aja, E. A., and Forns Contera, M.: *Actas dermo-sif.* **25**:103 (Nov.) 1932.
6. van Putte, P. J.: *Nederl. tijdschr. v. geneesk.* **79**:3031 (June 22) 1935.
7. Wendt, H.: *München. med. Wchnschr.* **85**:367 (March 11) 1938.
8. Scherber, G.: *Wien. med. Wchnschr.* **82**:841 (June 25) 1932.
9. Fasal, P., and Konrad, J.: *Med. Klin.* **33**:1360 (Oct. 8) 1937.
10. Grieco, V.: *Rev. Assoc. paulista de med.* **9**:63 (July) 1936.
11. Wendlberger, J., and Hrad, O.: *Dermat. Wchnschr.* **108**:125 (Feb. 4) 1939.
12. Harrison, L. W.: *Brit. J. Ven. Dis.* **15**:203 (July) 1939.

to this number, 49 patients were dropped from the series because of irregularity in attendance, and the results observed in them are not included in this study

An untreated group of patients with primary lesions, for whom a diagnosis of syphilis was established by dark field examination, received one intramuscular injection of acetylglycarsenobenzene and were immediately hospitalized to determine the effect of the drug on the disappearance of *Spirochaeta pallida* from the lesions. All other patients, also previously untreated, were ambulatory ones. In all cases general medical examinations were made, special attention being given to the eyes and to the cardiovascular and nervous systems.

Kahn tests were made on each patient at least once a month in the laboratory of the Falk Clinic of the University of Pittsburgh. The results obtained from this laboratory were checked with those recorded on the same blood specimen at two other laboratories, and there was little or no discrepancy in the comparative laboratory findings. The spinal fluid was checked for all patients except those who refused examination.

Of the total number of patients we are reporting on, 7 (8.2 per cent) have completed two years' treatment, 44 (52.4 per cent), eighteen months' treatment, 20 (23.4 per cent), twelve months' treatment and 14 (16.0 per cent), six months' treatment. When these were admitted to the hospital, in 48 the condition was latent, in 24 secondary and in 12 primary. We reiterate that none of the group had received anti-syphilitic treatment at any previous time.

The following routine course was used in all cases, regardless of the stage of syphilis. A dose of acetylglycarsenobenzene (6 cc for male and 4 cc for female patients) was given once weekly for six weeks, followed by one dose (60 mg of bismuth) weekly of an oil-soluble bismuth compound for six weeks and one dose weekly of mercuric salicylate (0.065 mg of mercury) for six weeks.

The acetylglycarsenobenzene was administered intramuscularly, deep into the upper and outer quadrant of the gluteus maximus. There were no complaints of pain or tissue damage in patients treated in our clinic, in fact, because of this, the patients preferred injections of acetylglycarsenobenzene to those of bismuth or mercury. All patients with late stages of syphilis received supplementary medication with saturated solution of potassium iodide by mouth. Treatment was continuous, without any intervals or rest periods.

BY-EFFECTS

After the intramuscular administration of acetylglycarsenobenzene, immediate reactions, such as nitritoid crises, nausea, gastrointestinal symptoms, abdominal pain, headache, weakness and collapse, were not

observed. Herxheimer reactions occurred only in cases of early secondary or late primary syphilis, but, as a rule, these reactions were mild and not accompanied by the customary nausea or fever, being characterized by overaccentuation of the lesions. In our early experience with acetylglycarsenobenzene we gave biweekly injections of full doses. We observed dermatitis in 8 persons, progressing to the exfoliative stage in 6. This led us to the conclusion that such frequent administration of this arsenical, even in smaller doses, is contraindicated. Subsequently, our technic of administration was modified, and only one injection per week was given, the dose never exceeding 6 cc. in seven days. After this change, several persons who previously exhibited dermatitis received small doses once a week without apparent by-effect and later tolerated the full therapeutic dose. However, in 2 of these cases the dermatitis occurred after use of the modified technic.

In several of the patients in whom dermatitis developed in the early period, patch tests with arsphenamine, neoarsphenamine and mapharsen produced positive reactions. Delayed reactions, such as encephalitis, changes in the optic nerve and renal, neuritic, purpuric or hemorrhagic encephalitis, were not observed. In no patients were there recurrences of lesions on the skin or mucous membranes after medication with acetylglycarsenobenzene.

The question of depression of the hemopoietic system was given appropriate consideration. Complete studies of the blood were made on patients who had been under treatment for at least six months. In several we demonstrated minor suppression of leukocytes, with diminution in the granular elements and platelets. However, in none of these did we see the concomitant symptoms associated with granulocytopenia, and treatment was continued without further clinical developments.

Routine urinalyses were made in all cases prior to each injection of acetylglycarsenobenzene or a bismuth or mercury compound. At no time was treatment discontinued because of abnormal urinary findings.

Of the 84 patients on whom this report is based, 9 showed toxic manifestations. In 6 cases we had to discontinue the administration of acetylglycarsenobenzene because of intolerance to the drug.

One man after four doses had mild transient jaundice, which disappeared on discontinuance of administration of the drug. Subsequent treatment with acetylglycarsenobenzene was tolerated without by-effect.

EFFECT ON ACTIVE LESIONS

Primary Lesions.—After a diagnosis of syphilis had been established through dark field examination, a group of patients presenting typical primary lesions were hospitalized. Immediately on demonstration of *S. pallida* in the lesion, the patient was given one intramuscular injection

of 6 cc of acetylglycysenobenzene. Dark field examinations were repeated at intervals until three negative results were obtained. Prior to each examination of material from the lesion, the deep surrounding tissues were compressed by firm pressure in an endeavor to bring

TABLE 1—*Results of Dark Field Examination of Patients with Primary Lesions Before and After the Administration of Acetylglycysenobenzene and Hospitalization*

Patient	Time	Results of Dark Field Examination	Comments
B S Negro	9 a m	Positive	Drug administered
	2 p m	Positive	
	6 p m	Positive	
	9 a m	Negative	
	1 p m	Negative	
	6 p m	Negative	
J T White man	9 a m	Positive	Drug administered
	7 p m	Positive	
	9 30 a m	Negative	
	1 30 p m	Negative	
	6 p m	Negative	
A J White man	9 a m	Positive	Drug administered
	2 30 p m	Positive	
	6 p m	Positive	
	8 30 a m	Few nonmotile organisms	
	1 p m	Negative	
	6 p m	Negative	
F L Negro	9 a m	Positive	Drug administered
	6 p m	Positive, poor motility	
	9 a m	Positive, no motility	
	1 p m	1 organism seen, no motility	
	6 p m	Negative	
	9 a m	Negative	
	1 p m	Negative	
L S Negro	9 a m	Positive	Drug administered
	5 30 p m	Negative	
	9 p m	Negative	
E R White man	9 a m	Positive	Drug administered
	6 p m	Negative	
	8 a m	Negative	
D G White man	9 a m	Positive	Drug administered
	2 30 p m	Positive	
	6 p m	Positive	
	9 30 p m	Positive	
	11 a m	Negative	
	4 p m	Negative	
	9 p m	Negative	

spirochetes to the surface. A résumé of our dark field findings in this group is given in table 1.

Secondary Lesions—One case of secondary syphilis presenting condylomas in which active spirochetes were demonstrated was included in this study (table 2).

It will be noted that in the 7 cases of primary lesions negative results of dark field examinations were obtained within the following time

intervals: in 1 case ten hours, in 1 eighteen hours, in 3 twenty-four hours, in 1 twenty-six hours and in 1 thirty hours. It is evident that in primary lesions the drug has a rapid destructive effect on the spirochetes. for in most instances the result was negative within twenty-four hours. Apparently, therefore, the action of the drug on primary lesions is comparable to that of arsphenamine, neoarsphenamine or mapharsen. Continuous observation of these patients demonstrated that there was no recurrence of cutaneous manifestations but that with continued treatment there was rapid retrogression of the lesions.

In patients with primary syphilis the following results of treatment on the serologic reactions and on disappearance of lesions were obtained: The lesion disappeared in an average time of nineteen and five-tenths days, or after an average of five and two-tenths injections totaling

TABLE 2.—*Results of Dark Field Examination of a Patient with Secondary Syphilis Before and After the Administration of Acetylglycarsenobenzene and Hospitalization*

Patient	Time	Results of Dark Field Examination	Comments
J. W. Negress	9 a. m.	Positive	Drug administered
	2:30 p. m.	Positive	
	6 p. m.	Positive	
	11 p. m.	Positive	
	10 a. m.	Negative	
	3 p. m.	Negative	Discharged
	9 p. m.	Negative	

31.2 cc., or 2.2 Gm., of the drug. The rapidity of the disappearance of lesions compared favorably with results reported as following the use of arsphenamine, neoarsphenamine and mapharsen. In 10 patients a negative Kahn reaction was obtained in an average of ten weeks. Only in 1 case were we unable to reverse the Kahn reaction in a patient who had been under treatment for more than fifty-two weeks.

EFFECT ON SECONDARY SYPHILIS

The following results of treatment in patients presenting secondary manifestations of the disease were obtained: The cutaneous manifestations were rapidly cleared, and in the majority of cases they disappeared entirely in an average of fourteen to sixteen days. On an average, treatment for twenty-two weeks was followed by a negative Kahn reaction, the shortest period of treatment resulting in a negative reaction being ten weeks and the longest thirty-four weeks. In 1 case there was a persistent positive Kahn reaction after fourteen months and in another after twelve months of treatment. A persistent weakly positive reaction was noted in a third patient after nine months of treatment.

In our series of 24 patients with secondary syphilis there was no instance of clinical or serologic relapse

EFFECT ON LATENT AND TERTIARY SYPHILIS

Under the heading of latent syphilis are included all patients who were asymptomatic on admission but in whom a diagnosis of syphilis was made from a positive reaction to a Kahn test of the blood during a routine check in any of the departments of the clinic. Furthermore, there are included in this group a few adults in whom a diagnosis of congenital syphilis was made.

The treatment of this group of 48 patients with acetylglycarsenobenzene was not more productive of reversals of the Kahn reaction than has been our experience with arsphenamine, neoarsphenamine or mapharsen. The total number of reversals of the Kahn reaction was 11, or about 22.4 per cent. Again, as in the cases of secondary syphilis, we did not encounter any serologic relapse in this group. However, none of these patients has had a rest period during which all medication was stopped, and as it is possible that in such a period there might be remissions, a conclusive statement cannot be made until further studies have been completed. It may be said at this time that lesions of the skin and mucous membrane apparently disappeared as rapidly after the administration of this drug as after that of the other arsenicals. It was not so much the object of our investigation to determine whether or not acetylglycarsenobenzene was a more effective drug than the recognized arsenicals as it was to determine if this preparation could be well tolerated when given intramuscularly over a long period. Continued intramuscular injections of acetylglycarsenobenzene over periods up to two years did not produce apparent tissue damage.

EXAMINATION OF THE SPINAL FLUID

The spinal fluid of 64 patients under treatment was examined. A number refused spinal puncture, and several objected to a second examination. However, 23 of the 64 patients were given a second examination. Of the 11 who had a positive result at the first examination, 6 had negative results at the second examination. In 5 persons whose spinal fluid gave a positive reaction on the first examination the reaction remained positive. Two patients whose spinal fluid gave a negative reaction on first examination had a positive reaction at the end of the two year period. The remaining 10 patients who had negative results at the first examination of spinal fluid had negative results at the second examination. It is interesting to note that there seems to be no correlation between the results of examination of spinal fluid and the Kahn reaction of the blood.

SUMMARY AND CONCLUSIONS

Acetylglycarsenobenzene (3,4'-diacetylamino-4 hydroxyarsenobenzene-2' sodium glycolate) has been studied for two years in the department of dermatology of the University of Pittsburgh. While some observers have previously given the preparation intravenously, our work has been confined to its intramuscular application. The clinical study was restricted to a selected group of patients who had never before received antisyphilitic treatment and in whose cases the diagnosis of syphilis was confirmed either by dark field examination or by serologic test. The spirocheticidal activity of acetylglycarsenobenzene is shown by its rapid effect on the spirochetes in the primary lesions and the

TABLE 3.—*Summary of Results of Two Years' Study*

Total patients treated.....	84
Total doses of acetylglycarsenobenzene.....	2,100
Total doses of bismuth compound.....	1,656
Total doses of mercury.....	1,432
Total patients with serologic reactions still positive.....	43
Total patients with negative serologic reactions.....	41
Total per cent of reactions rendered negative.....	48.9
Primary Syphilis	
Total number of cases.....	12
Positive Kahn reactions.....	2
Negative Kahn reactions.....	10
Per cent negative reactions.....	83.3
Secondary Syphilis	
Total number of cases.....	24
Positive Kahn reactions.....	4
Negative Kahn reactions.....	20
Per cent negative reactions.....	83.3
Latent Syphilis	
Total number of cases.....	48
Positive Kahn reactions.....	37
Negative Kahn reactions.....	11
Per cent negative reactions.....	22.9

prompt disappearance of secondary lesions. A reversal of serologic reactions from negative to positive after treatment has not been observed, nor has clinical relapse occurred. A recapitulation of our two years' study is shown in table 3.

A study of our data shows that the therapeutic results obtained with acetylglycarsenobenzene are approximately equivalent to the reported results with mapharsen. As to the comparative therapeutic efficiency, only years of continued use of the drug on a wider basis will yield convincing data.

The primary object of this study, however, was to ascertain if the drug could be given with comparative safety for a long time by the intramuscular route. After two years' observation, we believe that with reference to local tolerance this is established.

Nitritoid reactions did not occur, but exfoliative dermatitis was observed. The incidence of the latter was much greater than with other

known arsenicals. The high incidence of toxic manifestations other than dermatitis reported by a number of foreign observers has not been observed by us.

From our preliminary studies we believe that acetylglucarsenobenzene is not to be recommended for general use. The incidence of toxic manifestations, such as dermatitis, must be materially lowered. Perhaps, as in the case of arsphenamine, the manufacturers will be able to lower the toxicity by a modification of the chemical formula, so that eventually the drug may be administered with reasonable safety as well as with therapeutic effectiveness.

ABSTRACT OF DISCUSSION

DR HARRY M. ROBINSON, Baltimore. In my clinic at the University of Maryland acetylglucarsenobenzene has been under investigation for ten months. Patients have been treated with courses of twelve weekly intramuscular injections (each dose 6 cc [0.42 Gm]) alternating with twelve intramuscular injections of a 10 per cent solution of bismuth camphenilate in olive oil. There are no rest periods. All patients were ambulatory.

We have treated 88 patients, 7 white persons and 81 Negroes. Sixteen had primary syphilis, of whom 2 had negative serologic reactions, 36 had secondary syphilis, 19 had syphilis during pregnancy, in 5 of these the condition was in the early stages, and they are included in the group with early syphilis, and 19 had congenital syphilis, 3 in the early active stage, 3 in the early latent stage, 3 in the late active stage and 10 in the late latent stage.

In the patients with primary and moist secondary lesions, the spirocheticidal time varied from eight to one hundred and seventy hours.

Eleven patients with moist early lesions gave negative results on dark field examination in twenty-four hours or less, 4 in from twenty-five to thirty-six hours, 7 in forty-eight hours and 3 in seventy-two hours. Reversal of the serologic reaction in patients with early syphilis after the administration of acetylglucarsenobenzene was, in our experience, somewhat slower and less frequently accomplished than with other arsphenamine products.

The involution time of primary lesions averaged twenty-five and five-tenths days, and that of secondary lesions, eighteen and four-tenths days.

In this series there were no serologic or clinical relapses.

In the 10 cases of syphilis during pregnancy in which the outcome is so far known, there were a criminal abortion, a spontaneous miscarriage at seven months, a premature syphilitic stillborn child, a patient who died of hemorrhagic encephalitis at the sixth month of pregnancy and 6 viable children. Serologic tests for syphilis on the 6 viable infants seven to fourteen weeks after birth gave negative results, and there were no clinical signs of syphilis.

Like Dr. Guy and his co-workers, I am convinced that acetylglucarsenobenzene is a potent antisyphilitic drug, capable of intramuscular administration. However, equally important with its therapeutic potency is the question of its toxicity.

Local pain was not a serious factor. Mild gastrointestinal reactions occurred in 8 patients. One patient had slight albuminuria and microscopic hematuria after the seventh injection, this was observed during routine urinalysis. There was no clinical evidence of impairment of renal function. Treatment was discontinued. One week later the urine was normal. In a patient with hypertensive cardiovascular

disease, it seemed that precordial pain and dyspnea were precipitated by the drug, and treatment was discontinued. In 1 case jaundice appeared after the sixth injection. Treatment was discontinued, but later, after twelve weeks of bismuth therapy, the jaundice cleared up and treatment with acetylglycarsenobenzene was resumed without ill effects.

Studies of the blood were made for 30 patients before treatment and after the tenth injection, but none showed any abnormality. Icteric indexes were obtained for 8 patients at some time during the course of arsenical treatment but were within normal limits.

Fatal hemorrhagic encephalitis developed in 1 of the pregnant patients after the second treatment. At autopsy she was found also to have hypernephroma. Cutaneous reactions occurred in 5 of our patients. The eruption in 1 was eczematous, with about seven small lesions, limited to the buttocks, surrounding the sites of injections. Another whose eruption began on the buttocks later had lesions of the fixed type on the thighs and neck. A third patient had an erythematous eruption, especially marked about a vaccination scar and around the site of injection of the drug. There was a case of exfoliative dermatitis which began as a lichen-planus-like eruption and which, although no further arsenical was given, changed to an exfoliative dermatitis. I include in this group a fifth case, one of erythema of the ninth day.

In my experience, acetylglycarsenobenzene has adequate therapeutic efficacy, almost comparable to that of other arsphenamine products. Nevertheless, the advantage of the intramuscular route of administration would more than compensate for its slightly lower therapeutic efficiency were it not for the incidence of serious reactions observed. In the 172 patients of Dr. Guy's series combined with my own there were 16 actually or potentially serious reactions, including 1 death. This suggests that in its present form, at least, acetylglycarsenobenzene may be too reactive as an antisyphilitic drug, and further attempts should be made to change the drug in order to obviate these reactions.

DR. JOSEPH EARLE MOORE, Baltimore: We have used this drug at the Johns Hopkins Hospital and can confirm completely the report made by Dr. Guy.

The manner in which the study of this arsenical drug has been approached is a model of correct procedure. Not satisfied with the experimental data as to toxicity and therapeutic efficiency emanating from Germany, the pharmaceutical house interested in the drug has first carefully repeated these and other experiments in its own laboratories, and the results have also been checked in an experimental laboratory at the Johns Hopkins Hospital. Then, with no idea of releasing the drug for general use unless the laboratory data were confirmed by careful clinical experience, the cooperation of several large clinics, including that of the Johns Hopkins Hospital, was enlisted.

The fundamental idea justifying detailed study of this preparation was the fact that, except for sulfarsphenamine, it is the only trivalent arsenical drug capable of intramuscular administration. If it proved to be as good, or even not quite as good, from clinical standpoints of therapeutic efficiency and toxicity, as the trivalent arsenicals administered intravenously, a great step forward would have been made, because of the technical ease of its administration. Unfortunately, this proved not to be the case. Though it has a fair degree of therapeutic efficiency, the incidence of serious toxic reactions is so high as to make its further use impossible. Unfortunately, also, the serious reactions observed are of types which occur only in human beings, not in experimental animals.

In the combined series of 235 patients from the three clinics of the University of Pittsburgh, the University of Maryland and the Johns Hopkins Hospital, there have been 28 serious reactions. Sensitization dermatitis developed in 18 patients, arsenical jaundice in 3, blood dyscrasias of one or another type in 5, severe nephrosis in 1 and hemorrhagic encephalitis in 1, the last patient dying. This is an incidence of nearly 12 per cent of serious reactions, so far above that observed with other arsenical drugs as to justify the immediate abandonment of the use of this one.

Disappointing as this result may be, the search for a potent and safe arsenical drug for intramuscular administration should certainly continue.

DR WILLIAM H. GUY, Pittsburgh. It is my belief that the most valuable ingredient of any drug or manufactured substance is the integrity of the manufacturer. We have been delighted with the attitude of the firm that asked us to do this work. At no time has there been any suggestion of concealing bad results. They gave us the drug and told us, "Use it and tell us what you find out about it." Nor was any question raised when it was determined finally that the drug would be adversely recommended. I feel that one is justified under these circumstances in recommending that such a procedure be carried on in the investigation of drugs in the future.

ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS ITS TREATMENT WITH SULFANILAMIDE AND ALLIED PRODUCTS

UDO J. WILE, M.D.
Professor of Dermatology and Syphilology

AND
HERBERT H. HOLMAN, M.D.
Instructor in Dermatology and Syphilology
ANN ARBOR, MICH.

The cause of acute disseminated lupus erythematosus is still obscure. The clinical picture, characterized by septic temperature, prostration, leukopenia, splenomegaly, arthralgia, albuminuria, microscopic hematuria and an invariably fatal termination, offers at least suggestive evidence that infection, whether focal or systemic, is an important etiologic factor. This deduction, perhaps, offers more justification for the use of sulfanilamide and products allied to it in therapy than is found in many other conditions subjected to this therapy during the phase of hyperenthusiasm invariably encountered during the early use of any newly described therapeutic agent.

Conflicting reports are noted in the literature regarding the therapeutic efficacy of sulfanilamide in acute disseminated lupus erythematosus. Wollenberg¹ reported improvement in a case of exanthematous acute disseminated lupus erythematosus. Anderson² reported spectacular recovery in a case of acute disseminated lupus erythematosus in which dissemination occurred in a discoid type of lupus erythematosus after undue exposure to sunlight and during therapy with gold sodium thiosulfate. Abramowitz³ reported improvement in 3 cases of acute disseminated lupus erythematosus. Bloom⁴ reported indifferent results in 5 or 6 cases of lupus erythematosus. Sulzberger⁵ reported indifferent

From the Department of Dermatology and Syphilology, service of Dr. U. J. Wile, University of Michigan Medical School.

1. Wollenberg, R. A. C.: *Lupus Erythematosus Disseminatus*, Arch. Dermat. & Syph. **38**:295 (Aug.) 1938.
2. Anderson, H. F.: *Fulminating Acute Lupus Erythematosus Cured by Sulfanilamide*, Arch. Dermat. & Syph. **38**:621 (Oct.) 1938.
3. Abramowitz, E. W., in discussion on Wise, F.: *Discoid Lupus Erythematosus Undergoing Dissemination*, Arch. Dermat. & Syph. **38**:661 (Oct.) 1938.
4. Bloom, D., in discussion on Wise, F.: *Discoid Lupus Erythematosus Undergoing Dissemination*, Arch. Dermat. & Syph. **38**:661 (Oct.) 1938.
5. Sulzberger, M. B.: *Lupus Erythematosus Treated with Sulfanilamide*, Arch. Dermat. & Syph. **39**:610 (March) 1939.

results in 2 cases of discoid disseminated lupus erythematosus. Cornbleet⁶ reported poor results in the treatment of disseminated lupus erythematosus. Weiner⁷ reported the use of sulfanilamide in 4 cases of disseminated lupus erythematosus. The first case was one of dissemination of a discoid lupus erythematosus, which was controlled by sulfanilamide. The second case was one of exanthematous subacute disseminated lupus erythematosus, which was arrested by sulfanilamide therapy. The last 2 cases were examples of the exanthematous type of acute disseminated lupus erythematosus, which progressed to fatal termination in spite of sulfanilamide therapy.

We have been given the opportunity of observing the effect of sulfanilamide and allied products in 7 cases of acute disseminated lupus erythematosus.

REPORT OF CASES

CASE 1—E. T., a 22 year old white unmarried woman, entered the University Hospital on Sept 15, 1937. The history revealed that her eruption had persisted intermittently for five years, with onset usually in the summer and remission with the advent of winter. Two years prior to admission, the patient noted the appearance on her legs of large blisters, which had responded promptly to local therapy. The eruption which she presented on admission appeared first in May 1937, disappeared during June and July and reappeared in August, from which time it had persisted. She had been treated previous to admission with various ointments and lotions and also by ultraviolet irradiation, which made the lesions worse. Pain in the joints had been present for ten days prior to admission.

Initial examination revealed that the patient was well nourished and well developed but acutely ill. Her temperature was 100.2 F, her pulse rate 96 and her respiratory rate 24. Examination of the skin revealed an eruption confined to the head, neck, upper extremities and anterior surfaces of the legs. The face was universally involved by a purplish, dusky erythema, with superimposed coarse, easily removable scales. Vesiculation was present at the angles of the mouth. There was edema of the face and eyelids. This process extended down over the neck and involved the upper part of the chest. Seven eighths of the cutaneous surface of the arms was involved by discrete and confluent erythema with superimposed scales. There were also areas of loosely adherent, necrotic epithelium, which had apparently followed previous vesiculation. Some of these lesions presented impetiginous crusting. The extensor interarticular surfaces of the fingers presented dull erythematous macular lesions. The palms were involved by the erythematous scaling process present on the arms. The anterior surfaces of the legs showed discrete and confluent erythematous maculopapular lesions.

The mouth showed an inflammatory reaction in the gums but no ulceration. Pea-sized to bean-sized, nontender cervical and inguinal lymph nodes were palpable.

6 Cornbleet, T., in discussion on Ebert, M. H., and Omens, D. V. Lupus Erythematosus Disseminatus Subacutus, *Arch Dermat & Syph* **39** 372 (Feb) 1939.

7 Weiner, A. L. Disseminated Lupus Erythematosus Treated by Sulfanilamide, *Arch Dermat & Syph* **41** 534 (March) 1940.

The lungs were normal. The heart was not enlarged, and no murmurs were detected. The blood pressure was 125 systolic and 80 diastolic. The liver and spleen were not palpable.

Laboratory Studies.—The blood count studied at the Simpson Memorial Institute for Blood Diseases revealed 60 per cent (9.8 Gm.) hemoglobin by the Sahli method and 3,540,000 red blood cells and 2,650 white blood cells per cubic millimeter. A differential smear showed 74 per cent polymorphonuclear leukocytes, 8 per cent large lymphocytes, 3 per cent small lymphocytes and 15 per cent monocytes. The red blood cells were moderately irregular in size and shape but well colored. There were basophilic granulations in the leukocytes. The platelets were normal in number. The interpretation of this blood picture was "toxic depression of all the blood elements." The urine was normal. The Kahn test of the blood gave a negative result. The result of a tuberculin test was negative. Blood cultures were negative on September 17 and October 2.

Hospital Course.—The patient was slightly improved by bland therapy to the skin. Quinine sulfate was given for twelve days, without improvement, and its administration was discontinued owing to severe tinnitus. Up to this time the total white blood cell count had never been above 3,400 per cubic millimeter. The temperature ranged from 100.2 F. on admission to 103.8 F. on October 16.

Therapy with sulfanilamide was started on October 20. At this time, the patient was acutely ill. The skin, although the intensity of its reaction was considerably diminished, was still severely involved, particularly at the periphery of the previously involved areas. The borders of the older lesions were definitely elevated and acutely erythematous. Her temperature was 103.6 F., pulse rate 118 and respiratory rate 23. Between October 20 and 25 the patient received 20 Gm. of sulfanilamide. On October 21 the temperature reached a peak of 104.6 F. and then dropped abruptly to 98 F. on October 22, only to picket to 103.4 F. on the same day. The temperature returned to normal the following day. On October 24 the temperature reached a peak of 101.4 F.. The patient then received a transfusion of 500 cc. of whole blood. The next day the temperature was 99.4 F., and there was marked clinical improvement. The erythema in the skin faded perceptibly, and on October 28 the borders of the lesions were no longer elevated. The temperature was low until her discharge on October 31.

It was learned in a recent inquiry that this patient suffered a recurrence of her condition and died early in 1939. Unfortunately the circumstances which attended her demise could not be ascertained.

CASE 2.—O. B., an 18 year old single white girl, was admitted to the University Hospital on March 22, 1938, with an eruption which had its onset six weeks previously. At its onset the eruption was mildly pruritic and confined to the arms. It was treated by the application of dry calcium phosphate and by internal medication. While she was taking this medication the eyelids and surrounding skin became edematous and reddened, and the eruption on the arms, more extensive. It was noted at this time that the patient's finger tips became cyanotic while dependent. The patient added the information that this had occurred for as long as she could remember, particularly in cold weather.

In December 1933 a doubtful reaction to a blood test had been noted, and the patient had received considerable antisyphilitic therapy in the form of neoarsphenamine and thio-bismol. The Kahn reaction of the blood was negative in 1934 and remained negative. The family history was not significant.

Initial examination revealed that the patient was well nourished and well developed and did not appear acutely ill. The skin presented a generalized eruption which spared the legs. The eyelids were swollen and erythematous. On the arms, thighs and back the eruption was characterized by dull, blotchy maculopapular erythema, which in some areas formed noninfiltrated plaques by confluence of the papules.

General examination revealed acute tonsillitis and periapical abscesses. There was no lymphadenopathy. The heart and lungs were normal. The liver and spleen could not be palpated. The extremities appeared to be edematous but did not pit on pressure. Definite acrocyanosis was noted when the extremities were dependent for a short period.

Laboratory Studies—The urine was normal. Complete study of the blood, performed at the Simpson Memorial Institute for Blood Diseases, revealed 3,940,000 red blood cells and 5,200 white blood cells per cubic millimeter and 72 per cent (117 Gm) hemoglobin by the Sahli method. A differential smear showed 69 per cent polymorphonuclear leukocytes, 20 per cent large lymphocytes, 7 per cent small lymphocytes and 4 per cent monocytes. No eosinophils were seen, thus ruling out a previously tenable diagnosis of trichinosis. The platelets were adequate in number. The total white blood cell count never exceeded 8,600 per cubic millimeter.

Hospital Course—The patient was admitted to the dermatologic ward with a diagnosis of erythema multiforme and was given saline catharsis, calcium gluconate orally and bland therapy to the skin. With this regimen the skin showed definite improvement with the exception of the eyelids, which failed to respond to local therapy.

Shortly after admission the patient began to complain of generalized muscular aches and pain in the joints. The temperature was elevated almost constantly from March 27 to July 1, the day of discharge. The character of the temperature varied from constant elevation between 100 and 102 F to occasional picket fence type, with peaks of over 104 F.

On April 13 sulfanilamide therapy was instituted, and the patient received a total of 10 Gm of this drug, without any change in the clinical picture. The administration of sulfanilamide was discontinued on April 16.

On April 23 the administration of quinine sulfate was started, and some improvement was noted, in that pains in the muscles and joints partially subsided and the cutaneous lesions faded somewhat, although the erythematous puffiness around the eyes persisted and the temperature was still elevated. The dose of quinine was gradually diminished, and its administration was finally stopped on April 28, since the patient complained of tinnitus. At this time suggestive purpuric lesions were noted on the palms and soles. After this there was an exacerbation of the entire process, with increase in pain in the joints and in depth of erythema, and about this time edema of the vulva was first noted. Subsequent to this exacerbation the cutaneous lesions became definitely dusky in hue. The temperature remained elevated as high as 103 F. An abscessed tooth was removed, without any change in the condition. Quinine sulfate was again given for four or five days, without appreciable effect.

On May 18 a biopsy of muscle and skin from the thigh was performed, with the following report:

"The skin is without inflammatory foci. No vascular lesion is found. There are some edema and serous atrophy of the panniculus. The voluntary muscle shows no significant inflammatory infiltrations or vascular lesions. The changes seen do not suggest dermatomyositis. There is no evidence of trichinosis. The

muscle does show, however, other marked changes. There is some replacement by adipose tissue, and throughout the muscle there are a great many degenerating and atrophic fibers. Consideration of the muscle apart from the history would favor a diagnosis of some acutely progressing muscular dystrophy."

On May 25 the patient received her first intravenous injection of 10 mg. of gold sodium thiosulfate, with subsequent improvement in her condition. The erythema and puffiness of the face subsided to a great extent. The eruption on the body was characterized at this time by a brawny pigmentation with mild scaling. The site of the removal of tissue for biopsy failed to heal by primary intention but rather became a slough, which gradually granulated from the base. The edema of the vulva was decidedly diminished. During the next six weeks the patient received six intravenous injections of gold sodium thiosulfate, the maximum dose being 20 mg. Improvement continued with the exception of one slight exacerbation. The hair of the scalp fell out rapidly. The pigmentation of the skin began to fade slowly. The temperature assumed normal levels for short periods. On June 24 a blood culture showed no growth.

In view of the fact that the patient was unhappy and actually despondent over the long hospitalization, she was discharged for a short time on July 1, 1938. She never returned, as requested, for check-up examination. Information received recently from a capable dermatologist revealed that the patient consulted him for treatment of a cutaneous condition which he diagnosed as lupus erythematosus.

CASE 3.—M. S., a married white woman aged 47, entered the University Hospital on Nov. 22, 1938, as a private patient of one of us (U. J. W.). Her history revealed that the eruption had its onset in May. At that time the patient noted the appearance of split pea-sized to coin-sized erythematous maculopapular lesions on the face and arms. These lesions did not respond to local therapy. In September the patient consulted one of us (U. J. W.), who made a diagnosis of disseminated lupus erythematosus. She was given three intravenous injections of a colloidal gold preparation at weekly intervals. After these injections she suffered a general physical decline and was unable to travel to Ann Arbor, a distance of 20 miles (32 kilometers), for further treatment. She then received three or four intravenous injections of sodium thiosulfate. Three weeks prior to admission albumin was noticed in the urine. At that time the patient complained of non-inflammatory edema of the face. The albuminuria persisted during the ensuing three weeks and was associated with great prostration and an increase in the severity of the cutaneous manifestations. Two months prior to admission the patient complained of blurring of vision and headaches, which were usually relieved by acetylsalicylic acid. She was told then that her blood pressure was elevated.

The past history revealed the intermittent presence of migratory arthritis, with pain, redness and swelling involving the ankles, wrists, elbows, hips and fingers, on different occasions. The involved joints always manifested a residual deformity after the subsidence of the acute process.

Two years previous to admission roentgenologic studies revealed nonvisually ill. Her temperature was 98 F. on admission but became elevated to 100 F. during the first day in the hospital. Her pulse rate was 80 and the respiratory rate 20. There was a brightly inflammatory eruption involving the face, neck, chest, back, shoulders and arms. There were some fissuring and weeping on the

neck and definite edema of the neck, of the lower part of the face and of the eyelids. The forearms presented discrete crusted maculopapular lesions, 2 to 3 cm in diameter. There were some maceration and fissuring on the arms. There were no lesions on the mucous membranes.

The liver and spleen could not be palpated. Her blood pressure was 170 systolic and 110 diastolic.

Laboratory Study—The urine showed a 4 plus reaction for albumin and no sugar. Microscopic examination of the urinary sediment revealed 10 to 15 red blood cells, 20 to 25 white blood cells and 10 to 15 granular casts. A complete blood count revealed 78 per cent (11 Gm) of hemoglobin by the Sahli method and 4,200,000 red blood cells and 4,200 white blood cells per cubic millimeter. The red blood cells were normal in size, shape and color. A differential leukocyte count revealed 65 per cent polymorphonuclear leukocytes, 10 per cent eosinophils, 18 per cent lymphocytes and 7 per cent monocytes. The Kahn test of the blood gave a negative result.

Hospital Course—The patient was first treated with bland local therapy. She was examined in consultation with members of the department of internal medicine, and a diagnosis of acute glomerular nephritis was made. It was felt that sulfanilamide could be used, with careful observation of the patient's renal function. At that time urea clearance studies showed 50 per cent clearance. The patient received during the ensuing seven days 27 Gm of sulfanilamide. After three days of sulfanilamide therapy, with the sulfanilamide level of the blood 10.5 mg per hundred cubic centimeters, there was distinct improvement in the condition of the skin. The blood pressure was 145 systolic and 90 diastolic. On the sixth day of sulfanilamide therapy the urea clearance was reported as 36 per cent and the nonprotein nitrogen content of the blood was 35 mg per hundred cubic centimeters. The patient manifested some intolerance to the drug in the form of headache, nausea and cyanosis. The patient received quinine sulfate during the entire period of hospitalization.

Some improvement was noted in the renal status, as evidenced by a reduction in the reaction for albumin to 3 plus and a reduction in cellular content (0 to 3 red blood cells, 0 to 5 white blood cells and only occasional granular casts). The patient was discharged after eighteen days of hospitalization, with distinct improvement both in the condition of the skin and in general physical condition.

The patient suffered only one mild recurrence of symptoms in the last eighteen months.

CASE 4—J. C., a white housewife aged 27, entered the medical service of the University of Michigan Hospital on Dec. 6, 1938, with a chief complaint of cutaneous rash. The onset of her difficulty occurred four or five years previously, at which time she underwent a nasal operation which involved scraping of the nasal bones. Subsequent to this time she noted a slow, but steady, loss of weight from her normal weight of 140 pounds (63.5 Kg). Two years prior to admission there occurred progressive weakness and frequent episodes of sore throat of one or two weeks' duration and also multiple episodes of pain in the joints with local heat, redness and swelling, which lasted from a few hours to a few days and then disappeared without residual deformity. She noted a low grade fever associated with these episodes. Seven or eight months ago she first noted the appearance of a severe eruption on the face, neck and trunk. The eruption gradually subsided, but there remained in the flush area of the face a scaling erythema which persisted until the day of admission. During the spring and summer of 1938 she noted mild episodes of fever, and one month before admission

she suffered a severe recurrence of symptoms, which included fever, general malaise, mild headaches, rheumatic pains in the shoulders and other joints and severe edema of the hands and face, particularly in the periorbital regions. There was some diminution of vision. A sore throat appeared and was associated with a cough which was productive of small amounts of purulent sputum. Frequent epistaxes occurred. Her temperature ranged from 100 to 103 F. daily for one month prior to admission. There were also anorexia and occasional nausea and vomiting. Four days before admission the patient first noted pain in the lower part of the abdomen, which gradually localized to a point lateral to McBurney's point. She was treated conservatively for questionable appendicitis, and the abdominal pain gradually subsided. She received a blood transfusion one week before admission, without apparent benefit.

She had never had rheumatic fever or chorea. There was a history of pneumonia and of questionable meningitis when the patient was 2 years old, which left her partially deaf.

Examination on admission showed the patient to be both chronically and acutely ill. The temperature was 103 F., the pulse rate 100 and the respiratory rate 18. Her blood pressure was 110 systolic and 80 diastolic. The skin presented scaling erythema of the flush area of the face, in association with definite periorbital edema and erythema. Examination of the ocular fundi revealed toxic retinitis. The tongue was coated. The gums were red and swollen. There were gray, nontenacious exudates present in both tonsillar fossae. The pharynx was reddened and presented streaks of old blood on its surface. The thyroid gland was barely palpable. There were inconstant rales over the hilus and middle part of the right lung. The heart was not enlarged. There was a short systolic murmur at the apex. No diastolic murmurs were heard. There was exquisite tenderness and muscle spasm localized to a point below and lateral to McBurney's point. No masses or viscera were palpable. There was, on digital examination, tenderness high in the right vaginal vault. There was also tenderness on the right side on rectal examination. The lower extremities showed faint erythema and pretibial edema.

Laboratory Study.—Urinalysis on admission revealed a 3 plus reaction for albumin, 0 to 3 red blood cells, 10 to 15 white blood cells and no casts. A complete blood count revealed 65 per cent (10.6 Gm.) hemoglobin by the Sahli method and 2,590,000 red blood cells and 4,650 white blood cells per cubic millimeter. A differential smear showed 50 per cent polymorphonuclear neutrophils, 42 per cent lymphocytes, 2 per cent monocytes and 6 per cent myelocytes. The leukocytes were young cells. Platelets were numerous. A Kahn test of the blood gave a negative result. The nonprotein nitrogen amounted to 35.2 mg. per hundred cubic centimeters. The total amount of protein in the serum was 4.2 per cent, with 1.8 per cent albumin and 2.4 per cent globulin, producing an albumin-globulin ratio of 0.75. The carbon dioxide-combining power of the plasma was 35 volumes per cent. The plasma chlorides were estimated as 504 mg. per hundred cubic centimeters. Urea clearance test readings were 50 and 54 per cent, respectively. Blood cultures showed no growth on four occasions.

Hospital Course.—The patient's condition became exceedingly grave during her first few days in the hospital. The temperature remained septic. There were frequent episodes of emesis and blood-streaked expectoration. There was decided oliguria, with an output of about one-tenth the intake, which was largely parenteral. The patient was periodically irrational and on the third hospital day had a severe clonic convulsion, which endured for four minutes. Lumbar puncture was imme-

diately performed, and 15 cc of clear spinal fluid under 200 mm water pressure was withdrawn, which was normal. Immediate improvement followed this procedure, but in spite of this improvement, the patient was put on the "danger list."

Sulfanilamide therapy was first instituted on the fifth day in the hospital and the patient received 36 Gm of the drug during the ensuing nine days. Five days subsequent to the cessation of the first course of sulfanilamide the patient was symptomatically much improved, although the oral lesions persisted and were a source of great discomfort. The temperature remained septic. The facial and peripheral edema disappeared, and the erythema of the face partially subsided. The patient also received a transfusion of 600 cc of citrated blood after the administration of sulfanilamide was discontinued.

During the following two weeks the patient improved slowly but steadily. The temperature was never above 101.5 F, the white blood count had risen to 6,950 per cubic millimeter, and the urine showed no albumin and only 1 or 2 red blood cells. The erythema in the flush area disappeared almost completely, but occasional bullae appeared in the left axilla and on the buttocks. The oral lesions subsided almost completely. The phenolsulfonphthalein test of renal function demonstrated a 15 per cent return of function in the first fifteen minutes and a 25 per cent return at the end of one hour. In this interim the patient received another blood transfusion.

A second course of sulfanilamide therapy was instituted in the hope of producing even further improvement. A total of 79 Gm of sulfanilamide was given, and the sulfanilamide level in the blood was reported as 144 mg per hundred cubic centimeters. There was subsequent further decrease in temperature, but elevations to about 100 F occurred daily. The patient was able to leave her bed for short periods. A slight exacerbation in the cutaneous manifestations prompted further sulfanilamide therapy, 78 Gm was administered, with intolerance manifested in the form of almost constant nausea and headache. The sulfanilamide concentration in the blood was 102 mg per hundred cubic centimeters. The patient became afebrile and remained so in spite of the appearance of new ulcerative lesions on the tongue. These lesions disappeared without further therapy. The patient was then discharged, after being in the hospital ninety-eight days.

The patient was readmitted to the hospital one month later as an emergency patient. She had gained 15 pounds (7 Kg) up to ten days before admission. At that time she noticed the recurrence of pain, redness and swelling in the elbows, knees, fingers and toes. There had been severe pain in the right lower quadrant of the abdomen, associated with frequent vomiting. Examination revealed the patient to be acutely ill, with a temperature of 104.8 F, a pulse rate of 140 and a respiratory rate of 32. The blood pressure was 95 systolic and 40 diastolic. Erythema was present in the flush area of the face and also on the neck. There was an arcuate ulcer in the midline of the tongue. No murmurs were heard from the heart. There was dullness at the base of the right lung posteriorly, with moist rales, but no alteration in the breath sounds. The abdomen presented a boardlike rigidity, with tenderness throughout. The viscera could not be palpated. Rectal examination revealed a fluctuant mass on the right side. Analysis of catheterized urine revealed a 3 plus reaction for albumin, 30 to 40 red blood cells and 15 to 20 white blood cells and numerous granular and cellular casts. The total white blood cell count was 25,000 per cubic millimeter. The patient was immediately transferred to the surgical service, where a diagnosis of perforated appendix with generalized peritonitis was made. She was treated by the Ochsner regimen and given a 5 per cent solution of dextrose containing 5 Gm

of sulfanilamide intravenously. A roentgenogram of the chest showed pleuritis of the right base and apex, with probable pneumonitis or bronchopneumonia. The course was steadily downhill, with generalized convulsive seizures, cyanosis, oliguria and uremia, with the nonprotein nitrogen content of the blood 60 mg. per hundred cubic centimeters. Death occurred on the day after admission. Unfortunately, permission for autopsy could not be obtained.

CASE 5.—L. K., a 15 year old white boy, entered the dermatologic service of the University Hospital on March 25, 1939, with a chief complaint of "skin eruption." The eruption had its onset three weeks prior to admission as slightly pruritic, nonexudative, erythematous lesions, which gradually became more widespread until the entire face was involved in an erythematous, edematous process, so severe that at times both eyes were almost closed. Bullous lesions appeared in the mouth, ruptured and healed slowly. One week before admission the eruption spread to involve the dorsa of the hands, fingers and outer surfaces of the forearms. There were no pains in the joints or muscles. The patient described a similar attack in November 1937, which lasted about three and one-half weeks and which subsided after several blood transfusions.

There was a history of infantile eczema and of hay fever for five or six years. The family history was not significant.

Initial examination revealed the boy to be well nourished, well developed and taller than one would expect for his age. His temperature was 101.8 F., his pulse rate 112 and his respiratory rate 25. He presented an eruption confined to the face, the upper part of the chest and the arms. There was severe edema of the face, sufficient to almost close both eyes. The ears and lips were also distinctly edematous. The entire face, ears and V of the neck were characterized by the presence of a bluish red, dusky erythema, with superimposed fine, dry scales. On the dorsal surfaces of the arms and the upper part of the chest were numerous discrete, pea-sized to bean-sized, slightly raised, erythematous lesions, some of which appeared to be vesicular. The mouth presented numerous erosive and ulcerative lesions, with gray or yellow pellicles scattered over the hard palate, tongue and labial and buccal mucosae. The heart rate was rapid, and the first pulmonic sound was harsh, while the second sound was accentuated. A soft systolic murmur was heard over the apex. The blood pressure was 110 systolic and 60 diastolic. The liver and spleen were not palpable. The physical examination otherwise gave negative results.

Laboratory Study.—The urine was completely normal on admission and remained so until April 15, at which time there was a 1 plus reaction for albumin, no red blood cells or casts, and 2 to 3 white blood cells per high power field. A blood count showed 103 per cent (16.8 Gm.) hemoglobin by the Sahli method and 4,600,000 erythrocytes and 3,900 leukocytes per cubic millimeter. A differential smear revealed 64 per cent polymorphonuclear leukocytes, 34 per cent lymphocytes and 2 per cent monocytes. Platelets were abundant. During the course of hospitalization, in spite of blood transfusions, the hemoglobin dropped to 82 per cent (13.4 Gm.), and the total white blood cell count varied, attaining a peak of 9,300, but never dropping lower than the admission count of 3,900 per cubic millimeter. A blood culture was negative. A Kahn test of the blood gave a negative result. A roentgenogram of the chest revealed pleural thickening.

Hospital Course.—The patient received bland local therapy to the skin and a small blood transfusion. Sulfanilamide therapy was instituted on the fourth hospital day, and the patient received 22 Gm. in the next six days. Although the edema of the face subsided to a slight extent and the patient felt slightly

better, the temperature was elevated daily to 102 F. Purpuric lesions appeared on the arms and legs. His condition became slowly but steadily worse, with increase in temperature to 104 F. and the appearance of new lesions around the lips and in the mouth. He was presented at a meeting of the Detroit Dermatological Society, at which time the visiting dermatologists concurred in the diagnosis of acute disseminated lupus erythematosus.

Therapy with sulfapyridine was instituted on the eighteenth hospital day, and 21 Gm of this drug was given in the ensuing six days. Another blood transfusion was given during the course of sulfapyridine therapy. In spite of this medication the course of the patient continued to become steadily worse, with the continuous appearance of new lesions on the extremities, particularly on the tips of the fingers and toes.

The patient's family was informed of the serious nature of the illness but, in spite of this, insisted on the patient's discharge. He was discharged against advice after a hospitalization period of twenty-nine days, at which time his rectal temperature was 106 F.

Communication with the patient's local physician revealed that the course was steadily downhill, in spite of another blood transfusion. Death occurred six days after the patient's discharge. A blood culture taken shortly before death revealed a pure culture of *Streptococcus viridans*. Permission for autopsy was not obtained.

CASE 6—J. L., a 28 year old, married white man, entered the University Hospital on April 21, 1939, with a chief complaint of "kidney trouble." He had been well until two months prior to admission, at which time he noted the appearance of swelling around the eyes associated with an eruption which spread across the bridge of the nose onto the cheeks. The eruption persisted with slight dissemination so that the ears and upper part of the back were involved. Three weeks after the onset of the eruption, the patient first noted pains in both ankles, both knees and the muscles around both knees. He also noted a pain in the right lower quadrant of the abdomen, which radiated through to the back. He felt at this time that he was feverish, in that he perspired freely, particularly at night, and frequently awoke in the morning with his sleeping garments moist. He complained of occasional headache and ease of fatigue. Five weeks after the onset of the eruption he noted swelling of both ankles and knees.

The past history was not remarkable, with the exception of traumatic amputation of the entire left upper extremity when he was 5 years of age.

The patient had been married for eighteen months. His wife and a child, aged 7 months, were living and well. His family history was not significant.

Initial examination revealed that he was well developed and well nourished and appeared subacutely ill. The skin presented a discrete and confluent dusky erythematous eruption in a striking "butterfly" distribution on the nose and flush areas of the face, with extension around the eyes, on the forehead and on the ears. Scattered lesions were also noted on the upper part of the back. The lesions were maculopapular, varied in size from that of a glass pinhead to that of a dime and were covered with a fine scale. The erythema did not blanch entirely on pressure. There was edema of both eyelids, with faint erythema. Macular, purpuric lesions were noted on the hard palate. The tonsils had been cleanly removed.

General examination revealed generalized, nontender, bean-sized lymphadenopathy. The lungs were normal. The heart was not enlarged. No murmurs were heard. The blood pressure was 145 systolic and 90 diastolic. The liver and spleen could not be palpated.

Laboratory Study.—The urine on admission showed a 2 plus reaction for albumin, no sugar, 50 to 70 red blood cells, 10 to 15 white blood cells and 15 to 25 granular casts. The blood on admission revealed 78 per cent (11.4 Gm.) hemoglobin and 3,780,000 erythrocytes and 4,020 leukocytes per cubic millimeter. A differential smear showed 68 per cent polymorphonuclear neutrophils, 1 per cent eosinophils, 28 per cent lymphocytes and 3 per cent monocytes. The reaction to a tuberculin test with a dilution of 1:10,000 was negative after forty-eight hours. A roentgenogram of the chest was normal. The result of a Kahn test of the blood was negative. A blood culture showed no growth. The nonprotein nitrogen content of the blood was 41.3 mg. per hundred cubic centimeters on admission. The sedimentation index was 0.54 mm. per minute. A urea clearance test showed 24 per cent and 23 per cent clearance in two specimens.

Hospital Course.—The temperature was 99.5 F., the pulse rate 85 and the respiratory rate 20 on admission to the ward. There was daily elevation of temperature to 100 F. for several days. The patient was given a neutral diet, with 90 Gm. of ammonium chloride daily for three day periods alternating with three day rest periods. The nonprotein nitrogen content of the blood was 60 mg. per hundred cubic centimeters, and the carbon dioxide-combining power of the plasma was 31 volumes per cent on the seventh hospital day. The condition was diagnosed as acidosis and uremia following ammonium chloride therapy. Ammonium chloride therapy was discontinued, and the diet was changed to a salt-poor, low protein diet, and fluids were forced to 4 liters daily. It was deemed wisest to postpone sulfanilamide therapy until the nonprotein nitrogen content of the blood could be reduced. On the tenth day in the hospital the patient became comatose and disoriented, rallied temporarily after the administration of intravenous fluids and again lapsed into coma. The blood pressure was 170 systolic and 100 diastolic. Coma persisted in spite of all therapy, and the nonprotein nitrogen level of the blood rose to 120 mg. per hundred cubic centimeters. Five grams of sulfanilamide were given intravenously on the twelfth and fifteenth hospital days, since it was felt that the situation was hopeless and that nothing but good might be derived from this therapy. Coma persisted in spite of the sulfanilamide, and the course continued steadily downhill. The patient died on the twenty-first hospital day.

Permission for autopsy was obtained, and members of the department of pathology returned as preliminary diagnoses subacute glomerulotubular nephritis, anasarca, acute passive congestion of all organs, lipoidosis of the myocardium, kidneys and liver, far advanced bilateral acute fibrinopurulent lobular pneumonia, splenic and pulmonary infarcts, marked submucosal hemorrhage of the small intestine, acute hemorrhagic pharyngitis, chronic ulcer of the rectum and old calcified tuberculous hilar lymphadenopathy. There were no endocardial vegetations.

CASE 7.—I. E., a 19 year old single white woman, was admitted to the University Hospital on Sept. 12, 1939, with a chief complaint of "eruption on the face." She had enjoyed good health until three months prior to admission, at which time painful swelling of the proximal interphalangeal joints of the fingers first developed. Because of this, she consulted her local physician, who found albumin in her urine. The arthralgia of the finger joints was followed in three weeks by similar involvement in the wrists, shoulders and feet. These symptoms endured until one month prior to admission. The patient became progressively weaker. Iron and liver extract were administered to combat anemia which was present. Three weeks prior to admission pleuritic pain developed in the apex of the right lung, which gradually subsided. For three weeks prior to admission she had intermittently "cleared her throat" and expectorated bright red blood. Two weeks

before admission she first noted the appearance of the cutaneous eruption, which progressed gradually until the bridge of the nose and the cheeks were involved in a butterfly distribution. The ears and suprasternal region were also involved. There had been bleeding from the gums and subconjunctival hemorrhages for one day prior to admission.

There was a history of only measles, whooping cough and scarlet fever when she was 4 years of age. Her family history was not significant.

Initial examination revealed a well developed and well nourished woman who appeared acutely ill. The temperature was 102.2 F, the pulse rate 96 and the respiratory rate 20. Her blood pressure was 132 systolic and 70 diastolic. A dusky, blotchy, confluent, macular erythema involved the bridge of the nose and malar eminences in a typical "butterfly" pattern. Similar lesions were also present on the forehead, chin, upper part of the chest and back. The nasal mucosa presented several small areas of superficial ulceration. Both eyes revealed subconjunctival hemorrhages lateral to the corneas. The external appearance of the eyes was otherwise normal. The fundi were normal. The lips were dry and fissured. Evidence of hemorrhage was present in the gingival margins, which were edematous and congested. Petechiae were noted in the buccal mucous membranes, together with superficial ulcerations on the palate and uvula. The lungs were normal. The heart was normal in size. A third heart sound was audible over the apex. There was a soft, blowing systolic murmur heard over both the apex and the base. No diastolic murmur was heard. In the right upper quadrant of the abdomen there was slight tenderness without spasm. The liver and spleen could not be palpated. The reflexes of the upper extremities were sluggish, and those of the lower extremities could not be elicited. There was no edema of the ankle. The joints were normal except for slight tenderness during internal rotation of the shoulder joints. There was a slightly tender, enlarged, right axillary lymph node.

Laboratory Study—The result of a routine Kahn test of the blood was negative. Repeated urinalyses showed 1 to 3 plus reaction for albumin, occasional to 10 red blood cells, 10 to 15 white blood cells and 10 to 20 coarsely granular casts. A blood count, studied at the Simpson Memorial Institute for Blood Diseases, revealed 3,700,000 erythrocytes and 2,200 leukocytes per cubic millimeter and 59 per cent (9.3 Gm) hemoglobin. A differential smear showed 82 per cent polymorphonuclear leukocytes, 6 per cent large lymphocytes, 8 per cent small lymphocytes and 4 per cent monocytes. Platelets were decreased in number. These findings were interpreted as being secondary to depression of the bone marrow by toxemia.

These observations remained constant until death, at which time the total white blood count was increased to 8,050 per cubic millimeter. The clotting time, clot retraction time and bleeding time were normal. A blood culture on two occasions gave negative results. Sedimentation rate was 13 mm per minute. A urea clearance test showed 44 per cent and 31 per cent clearance. An electrocardiogram was not definitely abnormal.

Hospital Course—The patient received supportive therapy in the form of three blood transfusions, ferrous sulfate and supplementary vitamins. Sulfanilamide therapy was instituted on the sixth hospital day, and the patient received 7.5 Gm of this drug in the ensuing twenty-four hours. Severe nausea necessitated discontinuation of this medication. Therapy with promin⁸ was then started, and the

⁸ Promin is a sulfanilamide derivative developed by Parke, Davis & Co. It is p, p'-diaminodiphenylsulfone-N,N'-di-(dextrose sodium sulfonate).

patient received 32 Gm. of this drug by subcutaneous injection during the next five days. The concentration of promin in the blood reached a peak of 21.5 mg. per hundred cubic centimeters. Response to this medication was indifferent. There was, perhaps, slight improvement in the cutaneous manifestations. The temperature, however, continued to picket daily to 103 F. during the entire period of promin therapy. The spleen was palpably enlarged and tender for the first time on the twelfth hospital day. At no time did the heart show clinical evidence of endocarditis.

Sulfapyridine therapy was instituted on the fifteenth hospital day, and the patient received 13 Gm. of this drug in the next four days. No visible benefit accrued. The patient had great difficulty in ingesting the drug, due to the presence of ulcers in the mouth and throat which bled almost continuously. Blood study at this time revealed 2,200,000 erythrocytes and 4,900 leukocytes per cubic millimeter and 35 per cent (5.6 Gm.) hemoglobin. A differential smear showed 84 per cent polymorphonuclear leukocytes, 9 per cent large lymphocytes, 2 per cent small lymphocytes and 5 per cent monocytes. The red blood cells showed all signs of regeneration. Platelets were adequate. A hematocrit reading was 19.5 per cent. The mean corpuscular volume was 90 cubic microns. It was the opinion of the workers at the Simpson Memorial Institute for Blood Diseases that this blood picture represented hemolytic anemia, conceivably secondary to the sulfapyridine therapy. A transfusion of 650 cc. of citrated blood was given, but in spite of this, the patient's condition continued steadily downhill, and death ensued on October 4, the twenty-third hospital day.

Postmortem examination, limited to the thorax and abdomen, revealed acute tubular nephritis, multiple petechial hemorrhages on the mucous membranes, lungs, conjunctivas and dura, pulmonary edema, terminal bronchopneumonia, generalized hyperplastic lymphadenitis and fatty nutmeg liver.

COMMENT

Unfortunately, the effect of sulfanilamide as the sole therapeutic agent could not be evaluated, since many of the patients received concomitant therapy, such as blood transfusions, quinine or gold sodium thiosulfate. However, since the effect of sulfanilamide on certain of the patients was not beneficial in spite of the other agents utilized, it might be justifiably argued that sulfanilamide was of at least some value in those cases in which it was used in conjunction with other agents and in which definite clinical improvement was noted.

Definite clinical improvement was noted in cases 1, 3 and 4 during the administration of sulfanilamide. In case 3 only one transitory recurrence of symptoms has been noted in the eighteen months since discharge. Case 1 is the same case in which Wollenberg¹ previously reported benefit by sulfanilamide. Death occurred at a later date. In case 4 death was caused by what was probably a recurrence of acute disseminated lupus erythematosus, complicated by an acute condition of the abdomen. In case 2, in which a diagnosis of acute disseminated lupus erythematosus could not be definitely established, there was no improvement after sulfanilamide therapy, but some improvement followed the administration of

gold sodium thiosulfate. In case 5 death occurred after an average trial of both sulfanilamide and sulfapyridine, without any significant improvement. Death occurred in case 6 after a rather poor trial of sulfanilamide, necessitated by severely impaired renal function. In case 7, in spite of therapy with sulfanilamide, promin and sulfapyridine, death occurred. The toxic effect of the latter drug may have been a factor in the death.

It is of interest to note that the only established case of acute disseminated lupus erythematosus herein reported in which improvement has persisted following the use of sulfanilamide was one of the discoid type which had undergone dissemination during therapy with gold sodium thiosulfate. The large majority of cases in which improvement was reported following the use of sulfanilamide were also cases of dissemination of a previously discoid lupus erythematosus. Patients with the exanthematous type of acute disseminated lupus erythematosus occasionally manifested transitory improvement, but the great majority of them ultimately died.

Promin was used in 1 case in which sulfanilamide was not tolerated. Sulfapyridine was used in 2 cases in which sulfanilamide had previously failed therapeutically. Neither of these drugs was found to be of greater therapeutic value than sulfanilamide although promin was tolerated in a case in which sulfanilamide could not be used.

SUMMARY AND CONCLUSIONS

The therapeutic effect of sulfanilamide, sulfapyridine and promin (p,p'-diaminodiphenylsulfone-N,N'-di-[dextrose sodium sulfonate]) was observed in 7 cases of acute disseminated lupus erythematosus.

Sulfapyridine and promin produced no beneficial results, failing therapeutically where sulfanilamide had previously failed. These drugs were not used in cases in which sulfanilamide was beneficial.

While the results in general are discouraging the fact that some improvement was manifested in several instances when sulfanilamide was administered warrants its further use in cases of this type. It is certainly as efficacious as the accepted therapeutic agents for this morbid syndrome.

Relatively better results were obtained in cases of discoid disseminated lupus erythematosus than in cases of the exanthematous type of acute disseminated lupus erythematosus.

EXCRETION OF BISMUTH IN THE URINE OF PATIENTS TREATED WITH BISMUTH ETHYLCAMPHORATE

FRANCIS M. THURMON, M.D.

AND

NORBERT BENOTTI, M.S.

BOSTON

At the present time it is generally accepted that after the intramuscular administration of a bismuth compound a large portion of the absorbed metal is excreted in the urine and a smaller portion is excreted in the feces, while the remainder is retained in the tissues for varying periods. In general, it appears that the excretion of bismuth in the urine may be considered to be a fair index of actively circulating bismuth, and this is an indication of the rapidity of its absorption from the muscles. Cole and his co-workers¹ stated that a preparation which furnishes a more or less continuous daily urinary excretion of 2 to 4 mg. or more of bismuth is potentially a valuable antisyphilitic agent.

In choosing a bismuth preparation the physician should consider the indications for each particular patient. An approved aqueous solution of bismuth administered two or three times weekly produces a rapid effect. For a somewhat slower but efficient effect an approved oil-soluble preparation is recommended for five to seven day injection, while for an effect slow in building up but eventually sustained, oil suspensions of bismuth are given once weekly. The insoluble bismuth salts, however, are slowly absorbed and occasionally form reservoirs of bismuth within the muscle.

The physician in choosing a bismuth preparation, should consider that in general the more motile or more rapid the bismuth effect, the greater the potentially toxic effect. Thus, the dosage of the approved aqueous bismuth solution is usually smaller than that of an oil-soluble solution, while the insoluble bismuth in suspension carries the largest dose of all.

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From the Clinic of Dermatology and Syphilology of The Boston Dispensary, the Chemistry Laboratory of the Joseph H. Pratt Diagnostic Hospital and the Department of Medicine, Tufts College Medical School, units of the New England Medical Center.

1. Cole, H. N.; Sollmann, T.; Henderson, K.; Binkley, G. W.; Connors, H.; Cooper, G.; Lover, W. R.; Riechle, H.; Schwartz, W. F.; Seecof, D., and Sullivan, M.: Choice of Bismuth Preparation: Clinical Résumé of Excretion and Retention Studies, *Am. J. Syph., Gonorr. & Ven. Dis.* **23**:143-149 (March) 1939.

It would seem, then, in view of these well known and generally accepted facts, that an oil-soluble bismuth compound which is therapeutically efficient, which is of low toxicity, which is not sufficiently opaque to cast a shadow detectable by roentgen rays and which, as measured by urinary excretion, produces a rapidly rising peak and a sustained bismuth effect well within the accepted therapeutic range—these factors being true with a dose of 1 cc, or 40 mg, of elemental bismuth, at seven day intervals—merits attention. Bismuth ethylcamphorate is such a compound. The data herein presented are observations on the level of bismuth excreted in the urine of patients treated with this liposoluble preparation.

An earlier paper,² a clinical study of bismuth ethylcamphorate, indicated that the drug possessed valuable properties in the treatment of syphilis. In that paper it was stated that the drug possessed a low degree of toxicity for the human subject and that judging by its clinical effectiveness it appeared to possess an optimum rate of absorption and elimination. Continuous clinical experience with its use through the past six years has amply borne out those observations. The present communication on absorption and elimination indicates a rapid absorption and a sustained circulation of bismuth adequate to maintain anti-syphilitic levels of bismuth concentration in the body. The data show that a dosage of 40 mg of elemental bismuth at seven day intervals is sufficient to maintain adequate bismuth in the circulation over sufficient periods for maximum therapeutic effectiveness consistent with lowest toxicity. The data also show that a larger dose (2 cc) is well tolerated and without nephrotoxic or other unusual untoward effects.

DESCRIPTION OF DRUG

Bismuth ethylcamphorate is a liposoluble bismuth salt of ethyl camphoric acid, having the formula $(C_8H_{14}COOC)_3Bi$ (23.47 per cent bismuth). It melts at 57°C and is soluble in oil and oil solvents. The drug is a stable, clear, oily solution, each cubic centimeter containing 40 mg of elemental bismuth, 0.011 Gm of camphor and 0.025 cc of benzyl alcohol dissolved in sweet almond oil. Acute toxicity experiments using albino rats show the minimum lethal dose of bismuth ethylcamphorate to be 250 mg of metallic bismuth per kilogram of body weight.

METHOD AND MATERIAL

The determination of bismuth was performed by using the photoelectric colorimeter,³ which has been described. A suitable quantity of urine was wet

2 Thurmon, F. M. Bismuth Ethyl Camphorate. Clinical Observations on a New Oil Soluble Bismuth in the Treatment of Syphilis, *New England J. Med.* 215:315-321 (Aug. 20) 1936.

3 Benotti, N., and Thurmon, F. M. The Photometric Determination of Bismuth in Urine, *J. Invest. Dermat.*, to be published.

ashed, and the yellow color was developed by means of four times normal potassium iodide. The transmission of the solution was determined by a Cenco photometer. A calibration curve eliminates standards, and from the transmission percentage the number of milligrams of bismuth was obtained.

The patients used for the study consisted of 9 adults, of whom 7 were male and 2 female. Each patient was hospitalized for a minimum period of three weeks. Daily twenty-four hour collections of urine were made, and specimens were analyzed for the bismuth content. The first twenty-four hour period comprised the control specimen to make sure the urine did not normally contain bismuth. The regular hospital diet was permitted. The patients were allowed to be up and about within the confines of their corridor, but at no time during the study did they leave the hospital. In certain cases the fluid intake was limited to a minimum of 1,200 to 1,500 cc. per twenty-four hours. Roentgenograms of the sites of injection were made in several cases to determine whether the bismuth within the muscle was sufficiently opaque to cast a shadow.

Two patients received a single injection of 2 cc. each. One patient received a single injection of 1 cc., and in this instance the bismuth excretion was followed

Patients Treated with Bismuth Ethylcamphorate

Case Number	Sex	Age, Years	Weight, Pounds	Height, Inches	Treatment With Bismuth Ethylcamphorate
1	Male	31	150.2	61.0	Single injection of 1 cc.
2	Male	34	137.5	71.5	Single injection of 2 cc.
3	Male	47	168.5	66.5	Single injection of 2 cc.
4	Male	45	138.0	67.0	1 cc. each week for three injections
5	Female	53	163.9	64.2	1 cc. each week for three injections
6	Male	59	100.0	63.5	1 cc. each week for three injections
7	Male	49	142.2	67.0	2 cc. each week for three injections
8	Male	52	142.5	66.0	2 cc. each week for three injections
9	Female	48	163.4	67.0	2 cc. each week for three injections

through to its completion. Three patients received the 1 cc. dose at seven day intervals for three injections. Three patients received the 2 cc. dose at seven day intervals for three injections. These patients are listed in the table.

Observations on the fecal excretion of bismuth after the intramuscular administration of bismuth ethylcamphorate are reserved for a possible future publication. Most investigators regard this phase of the study of parentally administered bismuth to be of little consequence as compared with the importance of bismuth excreted in the urine.

ROENTGEN RAY STUDIES

Absorption from the site of injection in the gluteal muscle, as judged by the thinning of the roentgen shadow, could not be accomplished with bismuth ethylcamphorate, because the material was not sufficiently opaque to cast a shadow. In 16 instances roentgenograms of patients receiving bismuth ethylcamphorate failed to show bismuth deposits. In all cases the drug was injected into the gluteal muscle, and each roentgenogram included both buttocks, thus encompassing all sites of injection.

The roentgen ray factors used in making these exposures were a rotating anode tube, 75 kilovolts, 250 milliamperes, and distance, 36 inches (91 cm.), with the Patterson high speed screens.

Two typical case histories follow

CASE 8—Observations from Dec 12 through 27, 1939

Dec

- 12 Before treatment No roentgenographic evidence of bismuth deposit
- 13, 10 a m Bismuth ethylcamphorate, 2 cc, administered into right buttock
- 13, 3 p m Roentgenogram taken, with no evidence of bismuth deposit
- 20, 10 a m Bismuth ethylcamphorate, 1 cc, administered into right buttock
- 20, 10 a m Bismuth ethylcamphorate, 1 cc, administered into left buttock
- 20, 3 p m Roentgenogram taken, with no evidence of bismuth deposits
- 27, 10 a m Bismuth ethylcamphorate, 2 cc, administered into right buttock
- 27, 3 p m Roentgenogram taken, with no evidence of bismuth deposit

CASE 4—Observations from Dec 6 through 28, 1939

Dec

- 6 Before treatment No roentgenographic evidence of bismuth deposit
- 7, 10 a m Bismuth ethylcamphorate, 1 cc, administered into right buttock
- 7, 3 p m Roentgenogram taken, with no evidence of bismuth deposit
- 8, 3 p m Roentgenogram taken, with no evidence of bismuth deposit
- 11, 3 p m Roentgenogram taken, with no evidence of bismuth deposit
- 14, 10 a m Bismuth ethylcamphorate, 1 cc, administered into left buttock
- 14, 3 p m Roentgenogram taken, with no evidence of bismuth deposit
- 15, 3 p m Roentgenogram taken, with no evidence of bismuth deposit
- 18, 3 p m Roentgenogram taken, with no evidence of bismuth deposit
- 21, 11 a m Bismuth ethylcamphorate, 1 cc, administered into left buttock
- 22, 3 p m Roentgenogram taken, with no evidence of bismuth deposit
- 28, 3 p m Roentgenogram taken, with no evidence of any dense metallic substance in the buttocks

These roentgenograms for bismuth deposits were taken at sufficiently varying intervals to detect bismuth within the gluteal muscle had it been there as a metallic substance or as some intermediary compound of sufficient density to cast a shadow. In no instance was a shadow obtained. This seems to indicate an absence of visible bismuth reservoir at the site of injection and a degree of motility making bismuth readily absorbed and available to the tissues. That there is such motility is amply borne out by the data in this paper on bismuth excretion and perhaps, in part at least, explains the excellent therapeutic properties of this preparation.

EXCRETION STUDIES

The data on absorption and elimination of bismuth in the urine following clinical dosage of bismuth ethylcamphorate are illustrated in charts 1 through 9.

The daily excretion of bismuth in the urine of human beings after intramuscular injection of bismuth ethylcamphorate in doses of therapeutic order is characterized by promptness of onset, considerable daily irregularity and long duration.

CASE 1.—The patient received a single injection of 40 mg. of bismuth and within eighteen days excreted 36 per cent of the total amount injected. A twenty-four hour urine specimen obtained forty-two days after the injection of bismuth showed

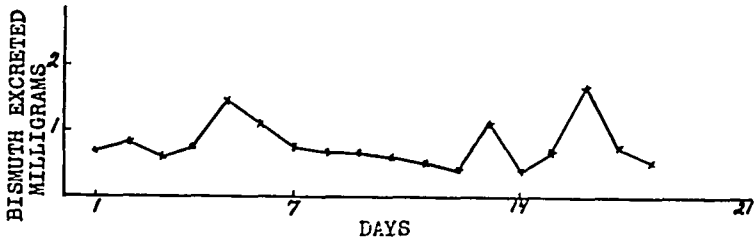


Chart 1 (case 1).—The daily excretion of bismuth in the urine after a single injection of 40 mg. of bismuth (1 cc. bismuth ethylcamphorate). The average daily excretion for the first week was 0.88 mg., for the second week 0.63 mg. and for the third week 0.92 mg. The patient excreted 36 per cent of the total bismuth injected within eighteen days after the treatment.

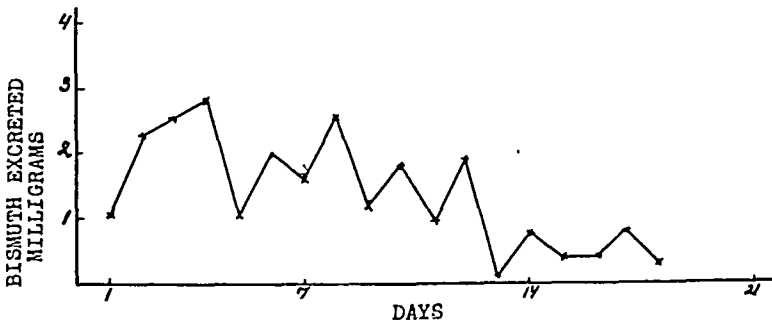


Chart 2 (case 2).—Within eighteen days after a single injection of 80 mg. of bismuth (2 cc. bismuth ethylcamphorate) 30 per cent was excreted in the urine. The average daily bismuth excretion for the first week was 1.79 mg., for the second week 1.32 mg. and for the third week 0.45 mg.

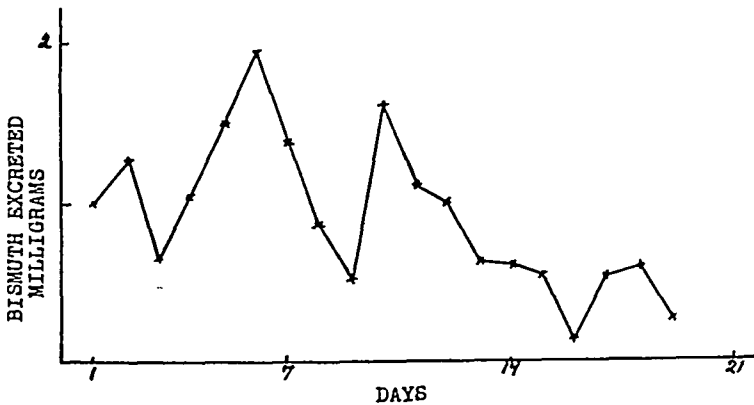


Chart 3 (case 3).—Within nineteen days after a single injection of 80 mg. of bismuth (2 cc. bismuth ethylcamphorate) 20 per cent was excreted in the urine. The average daily excretion of bismuth in the urine was 1.1 mg. for the first week, 0.92 mg. for the second week and 0.41 mg. for the third week.

0.075 mg. of bismuth per 50 cc. of urine. A second specimen, obtained fifty-six days after treatment, contained 0.035 mg. of bismuth per 50 cc. of urine. Another

specimen obtained fifty-six days after injection showed a trace of bismuth, while a final specimen obtained seventy-three days after the single injection showed no bismuth. The known sojourn of bismuth in the body in this particular instance was at least fifty-six days.

The day to day fluctuations of bismuth in the urine were considerable and tended to parallel the output of urine, although as a constant observation this did not hold true. The chart of case 6, amply illustrates this point.

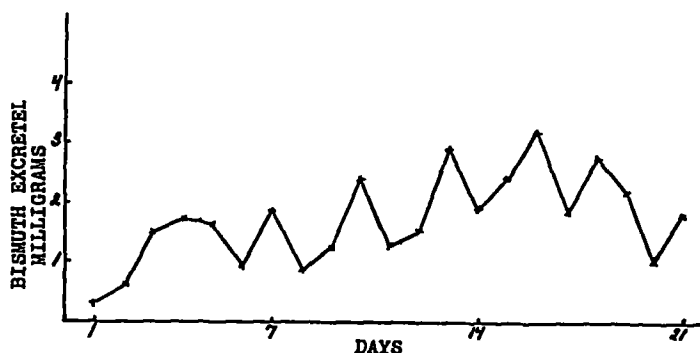


Chart 4 (case 4) —Within three weeks after three injections of 40 mg of bismuth (1 cc bismuth ethylcamphorate) at seven day intervals 30 per cent of the total bismuth was recovered in the urine. The average daily bismuth excretion for the first week was 1.23 mg, for the second week 1.73 mg and for the third week 2.21 mg.

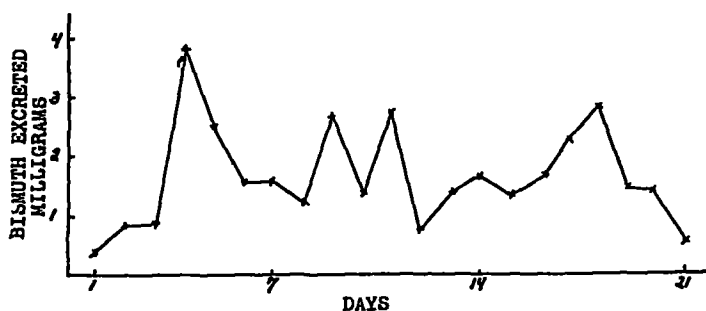


Chart 5 (case 5) —Single injections equivalent to 40 mg of elemental bismuth (1 cc bismuth ethylcamphorate) per week were given for three weeks, during which time 29 per cent of the injected bismuth was excreted in the urine. The average daily excretion of bismuth for the first week was 1.73 mg, for the second week 1.74 mg and for the third week 1.66 mg.

Peaks in the daily average bismuth excretion following single injections were usually attained in the first week and were followed by descending quantities over the study period.

CASE 2—After a single dose of 80 mg of bismuth there was an average daily excretion for the first week of 1.79 mg of bismuth, for the second week of 1.32 mg and for the third week of 0.45 mg.

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In contrast to this, the peaks in the daily average bismuth excretion of patients receiving multiple injections of 40 mg. and 80 mg. of bismuth at seven day intervals showed ascending levels of total or cumulative excretion, the maximum average being attained during the third week in 4 cases.

The total urinary excretion of bismuth in these cases ranged from 17 to 48 per cent within eighteen to twenty-one days following the first

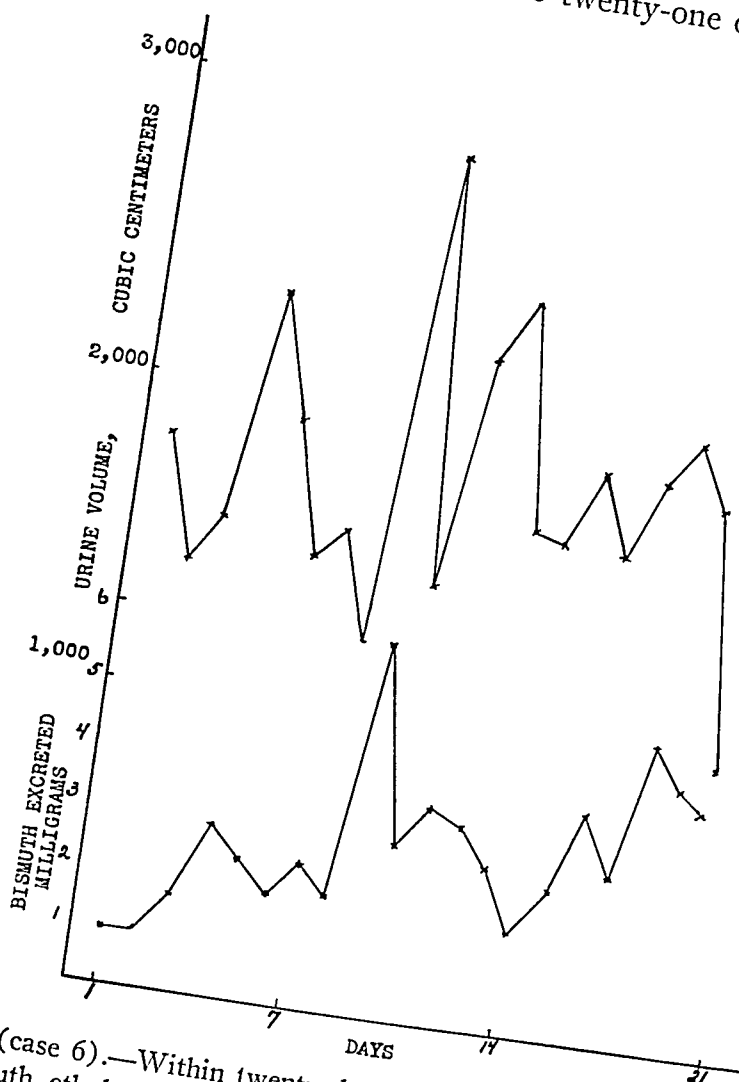


Chart 6 (case 6).—Within twenty days after the injection of 40 mg. of bismuth (1 cc. bismuth ethylcamphorate) each week for three weeks 48 per cent of the total bismuth injected was recovered in the urine. The average daily bismuth excretion was 1.8 mg. for the first week, 3.15 mg. for the second week and 3.72 mg. for the third week. The graph of the twenty-four hour urine volume is included to show that in some cases there is a tendency for the amount of bismuth excreted to follow in close relation to the volume of urine excreted.

injection, the average mean excretion being 29 per cent, regardless of dosage.

The average daily excretion of bismuth in urine usually varied directly with the dosage, after single injections and multiple injections.

In none of these patients was there evidence of nephrotoxic or other untoward effects

SUMMARY

A study was made of the daily excretion of bismuth in the urine of 9 adult patients after the intramuscular administration of clinical doses

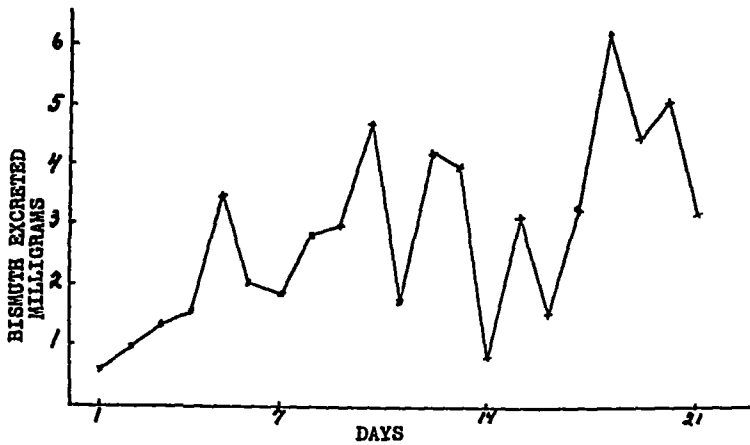


Chart 7 (case 7) —Injections of 80 mg of bismuth (2 cc bismuth ethyl-camphorate) were made each week for three weeks, during which period 25 per cent of the injected bismuth was recovered in the urine The average daily excretion of bismuth for the first week was 17 mg , for the second week 3 04 mg and for the third week 39 mg

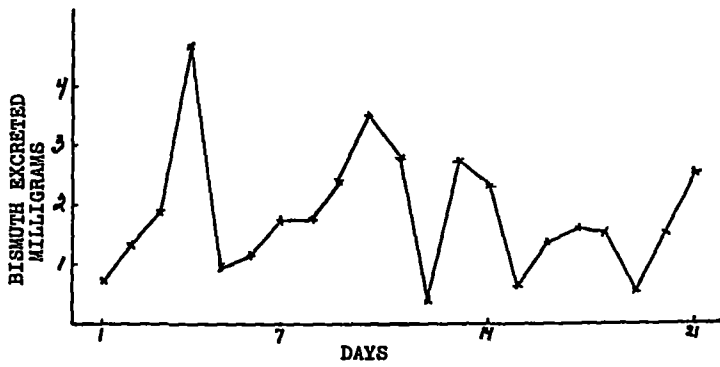


Chart 8 (case 8) —Injections of 80 mg of bismuth (2 cc bismuth ethyl-camphorate) were made each week for three weeks, during which period 17 per cent of the bismuth was recovered in the urine The average daily excretion for the first week was 184 mg , for the second week 231 mg and for the third week 147 mg

of an oil-soluble bismuth compound (bismuth ethylcamphorate), each cubic centimeter of which contains 40 mg of elemental bismuth

Three patients had only single injections, receiving 40 mg , 80 mg and 80 mg of bismuth, respectively Three patients received the 40

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mg. dose per week for three weeks, while a second group of 3 patients received the 80 mg. dose per week for three weeks.

In the 3 cases in which single injections were given the daily average bismuth excretion per week showed a maximum during the first week, with decreasing levels thereafter, in 2 cases, while in 1 case the average bismuth excretion per week resulted practically in a straight line.

In the 6 cases of multiple injections the daily average bismuth excretion per week showed ascending levels for each successive week, the maximum average excretion being attained in the third week, in 4 cases. In the fifth case the average daily bismuth excretion showed practically a straight line, while in the sixth case there was an ascending level which attained maximum excretion through the second week and was followed by a slight decrease through the third week.

One patient received a single injection of 40 mg. of bismuth and excreted 36 per cent of this bismuth in the urine within eighteen days.

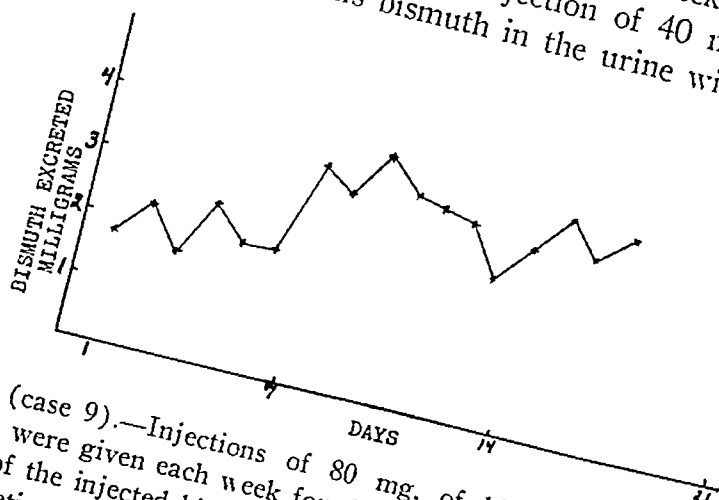


Chart 9 (case 9).—Injections of 80 mg. of bismuth (2 cc. bismuth ethylcamphorate) were given each week for three weeks; during the first eighteen days 26 per cent of the injected bismuth was recovered in the urine. The average daily bismuth excretion for the first week was 2.23 mg., for the second week 3.15 mg. and for the third week 3.4 mg.

Two patients each received single injections of 80 mg. of bismuth and excreted 29.5 and 20 per cent of this bismuth in the urine in eighteen and nineteen days, respectively.

Three patients received 40 mg. of bismuth each week for three weeks and excreted 48, 29 and 30 per cent of this bismuth in the urine in twenty, twenty-one and twenty-one days, respectively.

Three patients received 80 mg. of bismuth each week for three weeks and excreted 26, 25 and 17 per cent of this bismuth in the urine within eighteen, twenty-one and twenty-one days, respectively.

One patient received a single injection of 40 mg. of bismuth and had daily determinations of bismuth in the urine for eighteen days and thereafter at varying intervals until no further bismuth was excreted in the urine, the total observation period requiring seventy-three days.

Roentgenograms of the site of injection (gluteal muscle) at intervals varying from five hours to sixty days after the intramuscular administration of bismuth ethylcamphorate in all instances failed to show deposits of bismuth.

As judged by the average daily excretion of bismuth in the urine, the 2 cc dose (80 mg) of bismuth ethylcamphorate administered at seven day intervals is sufficient to maintain a sustained circulation of bismuth over a sufficient period of time to fall within the accepted standards of therapeutic effectiveness

The fecal excretion of bismuth is not reported

ACTION OF IODINE ON DISEASES OF THE SKIN AS INFLUENCED BY SEASON AND WEATHER

FREDERICK REHM SCHMIDT, M.D.
CHICAGO

The effect of the weather, climate and seasons on the incidence of cutaneous disease has recently been studied by Marchionini and Tor,¹ Walter² and myself.³ Clinical observations of this character have been amplified and substantiated by Petersen and Milliken,⁴ who have translated into terms of quantitative analysis the effect of fluctuations in barometric pressure, altitude and sunshine on the skin. These investigations have stimulated further study of the problem, with the purpose in mind of discovering the specific component in the environmental constellation that is responsible for the seasonal improvement noted in certain dermatoses.

In considering the effect of seasons and climate, dermatologists have realized that sunshine is not the only factor, for patients afflicted with atopic dermatitis or arthropathic psoriasis usually fare better in Arizona than in Florida. Beside such factors as the density of the air, humidity, pollens, fungi and temperature, there is the striking difference in altitudes between these two localities. At a medical meeting in Angora, Turkey, Fahri Izgi⁵ stated that in his opinion the rarity of neurodermatitis occurring on the plateau of Central Anatolia may be attributed exclusively to the altitude.

From the Northwestern University Medical School and the Outpatient Department of Grant Hospital.

Read at the Sixty-Third Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., May 30, 1940.

1. Marchionini, A., and Tor, S.: *Zur Klimatophysiologie und Pathologie der Haut*, Arch. f. Dermat. u. Syph. **179**:421, 1939.

2. Walter, F., in *Deliberationes Congressus dermatologorum internationalis IX-I Budapestini*, Sept. 13-21, 1935, Leipzig, Johann Ambrosius Barth, 1935, vol. 1, p. 323.

3. Schmidt, F. R.: *Skin Diseases and the Weather*, Arch. Dermat. & Syph. **32**:781 (Nov.) 1935.

4. Petersen, W. F., and Milliken, M. E.: *The Patient and the Weather*, Ann Arbor, Mich., Edwards Brothers, Inc., 1934-1937, vols. 1-4.

5. Fahri Izgi: *Spätexsudatives Ekzematoid Rost*, Dermat. Wehnschr. **108**:639 (June 3) 1939.

The air at high altitudes is less dense and contains relatively less oxygen. Duerst⁶ demonstrated that one way in which the body reacts to such an atmospheric environment is with stimulation of the thyroid gland. Increased amounts of thyroxine are released by the thyroid gland into the blood stream, from which a large portion is rapidly excreted in the urine and saliva. The fate of the residue of thyroxine will be considered later.

Not only does the average case of psoriasis show improvement at such altitudes, but it also shows improvement at lower altitudes during the summer months. The patient responds to both mountain and summer air with an increased production of thyroxine by the thyroid gland. Kendall and Simonsen⁷ showed that the thyroid gland of an animal contains over twice as much iodine in July as in February. Veil and Sturm⁸ demonstrated that a large part of this iodine is released in the blood stream, so that a higher iodine level is maintained in the blood in summer than in winter.

Any determination of the iodine content of the blood is open to criticism. A high level in the blood may merely indicate the passing of iodine from the thyroid gland on the way to its excretion in the urine or to its deposit in some tissue, where it will be stored until a metabolic demand is made on it.

A large portion of the iodine that is not excreted in the urine and saliva finds its way to the skin. Sturm and Buchholz⁹ and Wehren¹⁰ found that the skin and hair contain large amounts of iodine, of which some is constantly being withdrawn to satisfy its depletion elsewhere in the body. Another fraction is stored for future use, while the remainder is consumed in the process of tissue metabolism. Muller and von Fellenberg¹¹ showed that iodine is present in the skin in a biologically active form which is essential to the synthesis of protein.

The deduction that the content of cutaneous iodine also varies between summer and winter is inadmissible, for the data at hand pertain

6 Duerst, J. U. *Sauerstoffschwankungen der Atemluft in ihrer formbildenden Wirkung bei Mensch und Tier*, Berne, Paul Haupt, 1937.

7 Kendall, E. C., and Simonsen, D. G. *Seasonal Variations in Iodine and Thyroxine Content of Thyroid Gland*, *J. Biol. Chem.* **80**:357 (Dec.) 1928.

8 Veil, W. H., and Sturm, A. *Beiträge zur Kenntnis der Jodstoffwechsels*, *Deutsches Arch. f. klin. Med.* **147**:166, 1925.

9 Sturm, A., and Buchholz, B. *Beiträge zur Kenntnis des Jodstoffwechsels*, *Deutsches Arch. f. klin. Med.* **161**:227, 1928.

10 Wehren, E. *Ueber das Schicksal des Thyroxins im Organismus*, Zurich, Leemann & Co., 1939.

11 Muller, C., and von Fellenberg, R. *Untersuchungen über das Schicksal des Thyroxins im Organismus*, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **42**:661, 1932.

to the iodine content of skin obtained at autopsy. Sturm¹² pointed out that the microtitration of an amount of iodine less than 1 or 2 micrograms is difficult even when it is in solution; so the minute fraction of the element present in a small piece of skin has not been estimated.

A group of 74 patients with various chronic diseases of the skin were therefore subjected to iodine medication. The investigation extended over two years. Iodine was administered as the compound solution of iodine U. S. P. unless otherwise indicated. An average dose of 8 drops three times daily after meals was maintained until 1 to 2 ounces (30 to 60 cc.) had been taken. The blood pressure was recorded at each visit, but no surprising changes in the pressure were observed. There were no decided changes in the metabolic rate. No topical applications other than borated petrolatum were employed, and to this I attribute the fact that several patients failed to return for observation. No systemic or cutaneous symptoms of intolerance were found. Each case is selected as typical of a group of cases.

CASE 1.—A. W., a white man aged 28, presented himself in July 1938, with atopic dermatitis of ten years' duration. The condition of his skin was usually worse in hot, sultry weather. Scratch tests disclosed that his skin reacted strongly to dog's hair. When told of this the patient stated that he owned a dog at the time of onset of his cutaneous trouble but that he had not been near a dog since then. Attempts to desensitize him failed. He felt better after taking iodine in October, although the condition of his skin remained unchanged. The medication was repeated in July 1939, during a spell of hot, sultry weather. Itching soon grew more intense, and he stopped taking the medicine because the eruption began to spread over his body. There was slow improvement with a regimen of roentgen irradiation. Autohemotherapy failed to benefit the patient.

Four other patients with atopic dermatitis became visibly worse when iodine medication was instituted during hot, sultry weather. Each of these patients, however, had previously stated that such weather had always caused him great discomfort. Iodine was administered to the same patients in winter without exerting any visible influence other than producing slight subjective improvement in 3 of them. Five other persons with this disease did not respond clinically to iodine medication.

CASE 2.—A. W., a white woman aged 31, presented herself in 1934 with psoriasis of six years' duration. Topical applications and autohemotherapy had usually checked the spread of the eruption. The patient complained of frequent headaches. In December 1938 she was given iodine by mouth, without noticeable influence on the course of the disease. Returning in July 1939, during a spell of hot, sultry weather, she again took iodine. Seven days later she returned to say that she felt sick. She had a severe headache. The eruption had spread and pained her a great deal. Iodine medication was discontinued. A course of injections of whole blood seemed to arrest the progress of the disease. She soon felt much better. In March 1940 she returned to say that she had had the best winter for years. Her skin was comparatively clear.

12. Sturm, A.: Ein Beitrag zur Mikrojodtitration, *Biochem. Ztschr.* **200**:273, 1928.

CASE 3—J V, a white man aged 31, consulted me in May 1939, complaining of a widespread eruption and frequent headaches. A diagnosis of psoriasis was made. He had taken arsenic for the condition but had stopped doing so because it had made him sick. Autohemotherapy was employed, without benefit. In August, during a spell of hot, humid weather, treatment with a preparation containing 41 per cent of iodine combined with a fatty molecule was started. He took twelve tablets, returning to say that he "felt sick." The headaches had increased in intensity and frequency. Many red papules were distributed over the entire body. His accusation that the medicine had made him worse was unfortunately true.

CASE 4—M E, a white man aged 46, with psoriasis, had returned to me each winter for fourteen years for treatment which had never visibly benefited him. He again consulted me on Sept 18, 1939. For years he had noticed that the eruption grew worse with the onset of cool weather. At such times his hands hurt a good deal. His fingers were painful. On this occasion the palms were dotted with numerous, discrete, scaly maculopapules. The nails showed changes typical of psoriasis. He took 30 tablets of iodine in lipoidal combination. He stated that the pain in his hands had stopped two days after he had started taking the tablets and that he felt much better generally. On examination the palms were soft and only a few lesions were present. He remained relatively free from psoriasis until January 1940, when a fresh crop of papules appeared. The same organic preparation of iodine was again taken but failed to halt the progress of the disease. Autohemotherapy was employed, and involution of the lesions was noticeable after three weeks of treatment.

CASE 5—R M, a 55 year old housewife, first visited the outpatient department of Grant Hospital in September 1939. She complained of a generalized eruption of twenty years' duration. A diagnosis of psoriasis was made. She stated that the rash always grew worse with the onset of cold weather. She felt chilly. At this season her hands hurt a good deal. She was given iodine. A week later she felt much better and warm again. Her "rheumatism" had disappeared. No new lesions had appeared. Whole blood therapy was started in December. One cubic centimeter of a preparation containing casein and sodium iodohydroxyquinoline sulfonate was added to the blood before it was injected into the gluteal muscles. In February 1940 she felt well, and the rash looked better to her than when she had used ointments. Involution of many lesions had occurred. The scalp, which had been covered with scales, was greatly improved.

CASE 6—J O, a white woman aged 24, consulted me on Sept 24, 1939, for relief of psoriasis of ten years' duration. She had come to Chicago from Seattle, and the disease had steadily progressed throughout the summer. During the previous week she had suffered from headache, nausea and chilliness. The disease had lately appeared on the legs for the first time in her life. She was given iodine by mouth, returning three weeks later to say that she felt much better. The objective improvement was striking. Involution of most of the papules on the legs had occurred. No new lesions were observed. The older plaques on the back had cleared in the center. Autohemotherapy was employed in November, with considerable benefit.

These 5 cases were selected from a group of cases of psoriasis. An analysis of them shows that the patients usually responded unfavorably to the ingestion of iodine during hot, sultry weather in Chicago. At such times the entire level of iodine in the body is raised, necessitating

increased action of the adrenal gland in an attempt at compensation. The added increment of iodine at this season may suffice to upset the delicate mechanism of normal cornification.

The process of keratinization is intimately connected with the establishment of a proper balance between oxidation and reduction, for normal decomposition of the acid albumins of the nuclei cannot occur when the oxidation-reduction potential is disturbed. That this mechanism is of vital importance to the life of the skin has been established by Szent-Györgyi,¹³ Lewis,¹⁴ Radaeli¹⁵ and others. I¹⁶ found that the degree of oxidation varies in different parts of the skin, so that when iodine is taken up by the skin it is subjected to varying phases of oxidation and reduction.

The experiments of Müller and von Fellenberg¹¹ and numerous other investigators point to a close relation between iodine and the process of biologic oxidation. Shackell¹⁷ showed that the internal administration of thyroxin and iodine increases tissue oxidation.

Just as endogenous iodine stimulates cutaneous oxidation, so the application of iodine to the skin likewise stimulates the gas metabolism of the skin. Sametinger¹⁸ demonstrated that the rate of oxidation and the formation of carbon dioxide were both increased after the application of the tincture of iodine to a dog's skin. The absence of any appreciable redness or swelling of the painted area seems to exclude the presence of inflammation sufficient to cause such an acceleration of the gas metabolism in the skin.

The striking influence on the course of psoriasis when iodine was administered during the autumnal equinox is illustrated in cases 4 and 5. At such times iodine in the blood is starting to fall to its winter level, so that by late winter the body has lost a good deal of iodine. Iodine medication during this season may therefore supply a definite need and act as a catalyzer to stabilize cutaneous metabolism.

Many patients complained of frequent headaches and chilliness of the skin. Headache is regarded by many authorities as the most com-

13. Szent-Györgyi, A.: Mechanism of Biological Oxidation, Proc. Inst. Med. Chicago **12**:418 (Oct. 15) 1939.

14. Lewis, T.: Anatomy and Physiology of the Capillaries, New Haven, Conn., Yale University Press, 1929.

15. Radaeli, G.: Das Oxydations-Reduktions-Potentiale und die reduzierenden Prozesse in der lebendigen Haut, Arch. f. Dermat. u. Syph. **178**:253, 1938.

16. Schmidt, F. R.: Blood and Oxygen Supply of the Skin, Arch. Dermat. & Syph. **32**:576 (Oct.) 1935.

17. Shackell, L. F.: Biologic Assay of Thyroid, U. S. P., by Determination of the Oxygen Consumption in the Guinea Pig, J. Pharmacol. & Exper. Therap. **60**: 117, 1937.

18. Sametinger, E.: Die Wirkung von Jodtinktur auf den Sauerstoffverbrauch und auf die Durchblutung der Haut, Arch. f. exper. Path. u. Pharmacol. **159**:1, 1931.

mon clinical indicator of autonomic instability. It is of interest that it was in just such persons that iodine medication proved harmful during hot weather and beneficial at the equinox. These are persons who generally react to barometric fluctuations with headache (vasospasm) and disturbances of cutaneous sensation. These autonomically unstable persons are poorly buffered chemically in respect to calcium, phosphorus, chlorides and iodine. The reaction of the tissues easily becomes acid, and iodine is lost from the body during such periods of meteorologic unrest as the autumnal and the vernal equinox in Chicago.

Case 6 illustrates the possible fate of a psoriatic patient transferred from a favorable climate to one relatively unfavorable. The extent to which such a person reacts to environmental change is also conditioned by his state of autonomic stability. His degree of adjustment to climatic disturbances is thus strictly limited.

From these studies it appears that iodine is best administered to patients with psoriasis in spring and fall, at a time when the body is starting to lose iodine and electrolytes, such as calcium and phosphorus. Its administration during hot, sultry weather was found harmful. In winter it was without visible effect. Injections of whole blood during summer and winter, as a form of "interval" treatment, generally proved efficacious in arresting the progress of the disease. Cases 2, 4, 5 and 6 illustrate this point.

Several theories may be advanced to explain the action of autohemotherapy in psoriasis. The physiologic process of cornification is dependent on, among other factors, the normal fermentation of enzymes in conjunction with an undisturbed glycogen metabolism. The evidence at hand points to the assumption that the formation of such enzymes as tyrosinase and reductase is controlled by the autonomic nervous system. Numerous investigators have shown that nonspecific, alterative treatment, such as autohemotherapy, stimulates the autonomic nervous system. In this way the abnormal sequence of events leading to parakeratosis may be halted and order be restored, with normal keratinization as the result.

The second prerequisite for abnormal keratinization is a disturbance of glycogen metabolism. It has been known for a long time that the administration of iodine leads to mobilization of hepatic glycogen, thus increasing the supply of glycogen available for cellular synthesis.

Another way in which whole blood therapy may bring about involution of psoriasis is by altering the hydrogen ion concentration of the skin. Dziulikowska¹⁹ recently demonstrated that nonspecific treatment of this character induces phases of cutaneous alkalinity. In winter the

19 Dziulikowska, C. Ueber den Einfluss der physikalischen und chemischen Reize auf die Wasserstoffionenkonzentration der Haut, *Arch f Dermat. u Syph* 178 673, 1939

body tissues grow increasingly more acid with the approach of spring, owing to longer and more frequent periods of spasm and anoxemia that are caused, to a large extent, by meteorologic unrest. Autohemotherapy may thus act to reduce this acidity.

The specific manner in which alkalinity apparently stops parakeratosis may lie in the restoration of an optimal environment for the process of fermentation. The precept of Unna to treat patients with psoriasis with alkaline remedies finds support in the experiments of Wense,²⁰ who observed that the enzymatic action of such a ferment as tyrosinase is carried on best at a p_H of 7.6 to 8.

Swartz²¹ obtained cures in 2 of 8 patients with psoriasis treated with inhalations of ethyl iodide. My results were not so favorable, for I do not recall a single cure obtained with iodine medication in this series of cases. The dosage or the form in which the iodine was administered may have been inadequate. I am now using thyroxin in tablet form and believe that the results are better. Müller and von Fellenberg²² observed that potassium iodide is neither stored in the skin nor chemically bound to protein to the extent that thyroxin is.

The administration of an iodide combined with a fatty molecule, such as brassidic acid, to some patients was done for two reasons. Loeb and Velden²² showed that this preparation exerts great lipotropic action, which seemed important in the treatment of psoriasis. Secondly, a patient can thus be maintained for a longer time under the influence of iodine, because its elimination is slower than that of the alkaline iodides.

CASE 7.—M. K., a white woman aged 32, presented herself at the Northwestern University Medical School in March 1939, complaining of loss of hair over the entire body. Hair first fell out in patches on the scalp in the third month of pregnancy in April 1938, and by October complete loss of hair had occurred. She had frequent headaches. Slight exophthalmos was present. The basal metabolic rate was plus 12 per cent. The scalp was sensitive to touch. The patient had received ultraviolet irradiation, without benefit. She was given iodine by mouth. On July 14, 1939, after having taken 2 ounces (60 cc.) of compound solution of iodine U. S. P., she stated that she felt much better. The scalp was not sensitive to touch. Hair was starting to grow in patches. By October she was able to discard her wig, because hair was appearing over the entire scalp. In February 1940 she felt well, and there were no areas of alopecia.

The pathogenesis of alopecia areata is intimately connected with spasm of the terminal blood vessel of the hair papilla. As evidence of the danger to which the vitality of the hair is subjected by such spasm

20. Wense, T.: Ueber die Wirkung des Acetaldehydes auf die Haut, Arch. f. Dermat. u. Syph. **179**:136, 1939.

21. Swartz, J. H.: Treatment of Fungous Infections with Ethyl Iodide Inhalations, Arch. Dermat. & Syph. **40**:962 (Dec.) 1939.

22. Loeb, O., and Velden, R.: Ueber die Grundlagen der internen Therapie mit Jodfettsäurederivaten, Therap. Monatsh. **25**:209, 1911.

and anoxemia, Levy-Franckel and Cailliau²³ pointed to the diminished number of capillaries in areas of alopecia areata. They also stressed the frequency with which such loss of hair is associated with diseases in which the autonomic nervous system is involved, for example, exophthalmic goiter, scleroderma and vitiligo.

Petersen demonstrated that the vasospasm present in this disease can be induced by sudden changes in the barometric pressure. The spasm, with its attendant anoxemia, following in the wake of a rapid drop in temperature, may be of short or long duration, thus explaining the numerous clinical variants. Any agent that helps prevent or overcome spasm may be assumed to restore the normal mechanism of biologic oxidation. Such an agent is iodine. Guggenheimer and Fisher²⁴ showed that iodine, even in minimal doses, causes demonstrable vasodilatation of the peripheral blood vessels.

Considerable experimental data have accumulated to support the clinical observation that the growth of hair is influenced by seasonal, climatic and meteorologic factors. As previously stated, a large residue of the iodine released by the thyroid gland is ultimately stored in the hair. The presence of such relatively large amounts of iodine in the hair of animals which are producing great amounts of thyroxine under the stress of meteorologic unrest may explain the fact that hair grows faster in such animals.

Goldsmith²⁵ obtained good results with iodine medication in persons suffering from senile pruritus. Alleviation of itching in this condition may be attributed in a similar manner to improved tissue oxidation induced by vasodilatation. Substantiation for this hypothesis may be found in my observation in this series of cases that patients with senile pruritus associated with arteriosclerosis did better on iodine medication than those in whom no hardening of the vessels was detected clinically.

SUMMARY AND CONCLUSIONS

Iodine was administered to 74 patients suffering from various diseases of the skin uncomplicated by infection with fungi.

Psoriasis, alopecia areata and certain forms of pruritus were found especially responsive to iodine.

The type of reaction to iodine medication in one and the same person varied at different seasons.

23 Lévy-Franckel, A., and Cailliau, F. *Recherches sur le mécanisme physiopathologique de la pelade*, *Ann de dermat et syph* 6: 391 (May) 1935.

24 Guggenheimer, H., and Fisher, I. L. *Die Wirkung des Jods auf Herz und Gefass-system*, *Ztschr f d ges exper Med* 58: 196, 1927, *Med Klin* 23: 385 (March 18) 1927.

25 Goldsmith, W. N. *The Significance and Treatment of Itching*, *Practitioner* 142: 36 (Jan) 1939.

The degree of this reaction appeared to be conditioned by the relative stability of the person's autonomic nervous system. Patients possessing an unstable autonomic system reacted excessively to the administration of iodine.

Seasonal, meteorologic and climatic factors apparently determine the action of iodine on the course of cutaneous disease.

It is hoped that this investigation will stimulate further work in this field.

ABSTRACT OF DISCUSSION

DR. M. F. ENGMAN JR., St. Louis: This paper is an approach to a fundamental problem that has been given little attention in the past, and I hope that it will stimulate more work along the same line.

I believe that all physicians have noticed that changes in barometric pressure, temperature and seasons have a profound effect on disease. There are certainly days and weeks in which a particular disease will be worse or better. I think this is particularly true of eczema and neurodermatitis (atopic dermatitis). As an example of the effect of seasonal and environmental changes affecting chronic diseases, I offer acne vulgaris. During the summer acne usually clears up. Then in the fall the acne begins to get worse, and I think the peak of severity is reached some time around Christmas.

CUTIS VERTICIS GYRATA AND ACROMEGALY

ERWIN P ZEISLER, MD

CHICAGO

AND

LESTER M WIEDER, MD

MILWAUKEE

The morphologic changes in the scalp which characterize cutis verticis gyrata were first described by Robert¹ in 1848 and by McDowell² and Cowan³ in 1893 in microcephalic idiots. It was not until 1906 that Jadassohn⁴ called to the attention of dermatologists the condition which in the following year was given its present name of cutis verticis gyrata by Unna⁵.

During the ensuing twenty-five years Stratton⁶ found that 158 cases of this condition had been reported by European physicians. Many of the earlier observers, basing their opinions on clinical and histologic studies in single cases, concluded that the condition was due to postinflammatory changes, nevroid infiltrates and tumors, depending on the type of change met within their personal experiences. This confusion led Fischer⁷ to attempt to classify the condition according to its causes, and his classification has generally been accepted as a workable one by subsequent observers.

Fischer stated the belief that true cutis verticis gyrata occurs as a developmental anomaly, probably atavistic in type, representing a reversion to a lower form of life in which the muscles of the scalp could move it at will. This is probably the type originally described as present in microcephalic idiots, but a definite statement cannot be made without knowledge of the pituitary status, as determined by modern diagnostic study. For examples of the atavistic type, one might quote Charles Darwin, who described an arrangement of the skin of the scalp and even of the face in primitive African and Melanesian tribes which corresponds to later clinical descriptions of cutis verticis gyrata and closely

Read at the Sixty-Third Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., June 1, 1940

1 Robert, J. *de chir* **1** 125, 1848

2 McDowell, T. W. *J Ment Sc* **34** 62, 1893

3 Cowan, J. J. *J Ment Sc* **34** 539, 1893

4 Jadassohn, J. *Verhandl d deutsch dermat Gesellsch* **9** 451, 1906

5 Unna, P. *Monatsh f prakt Dermat* **14**:227, 1907

6 Stratton, E. K. *Cutis Verticis Gyrata. Report of a Case*, *Arch Dermat & Syph* **27** 392 (March) 1933

7 Fischer, J. *Arch f Dermat u Syph* **141** 251, 1922

simulates the furrowed skins of certain lower animals. Fischer regarded the conditions in all other cases as being diseases of the scalp "in the form of cutis verticis gyrata" and classified them as to their causation, as determined by histologic study, for instance, as (1) inflammatory diseases, acute or chronic, (2) anomalous and apparently congenital hypertrophies of the connective tissue, (3) tumors, such as cerebriform nevi and neurofibromas, and (4) changes in the scalp occasioned by proliferation of tissue in systemic diseases, such as myxedema, acromegaly, leukemia and cretinism.

Although cases of cutis verticis gyrata in association with acromegaly had been observed and described in the literature, including that of America, or presented before medical societies previously, Weber⁸ in 1928 stressed the relation in an article and tabulated 12 cases which had been studied by other observers. This author concluded that the excessive thickening of the connective tissue of the skin, which is not only too thick but too large for the skull, produces the characteristic gyri. Subsequently this association received more attention, especially in the Scandinavian literature, as the result of studies by Renander⁹ and Grönberg.¹⁰ The latter stressed the leonine aspect of the forehead and feet, as well as other clinical and roentgenologic evidences indicating an endocrine dysfunction closely akin to acromegaly, and gave the syndrome the title "megalia (hyperplasia) cutis et osseum." To the best of our knowledge, the cases herein reported constitute the third and fourth cases of cutis verticis gyrata associated with pituitary disease in the American literature, the first having been reported by Sisson¹¹ and the second by Cushing and Davidoff,¹² who gave the disorder the title "bulldog scalp." It is significant that brain surgeons occasionally have encountered this anomaly of the scalp accidentally in the course of operations on the pituitary gland. Also, many competent internists and endocrinologists are unaware that this condition is an important diagnostic clue to an underlying endocrine disturbance, without other outward prominent evidence of the disease, as illustrated in the account of case 2. These facts have stimulated the preparation of this clinical report.

8. Weber, F. P.: Brit. J. Dermat. **40**:1, 1928.

9. Renander, A.: Acta med. Scandinav. **67**:24, 1927; **96**:186, 1938; Acta radiol. **9**:399, 1928; **18**:653, 1937; **19**:254, 1938.

10. Grönberg, A.: Acta med. Scandinav. **67**:24, 1927.

11. Sisson, R. J.: Cutis Verticis Gyrata, J. A. M. A. **86**:1126 (April 10) 1926.

12. Cushing, H., and Davidoff, L. M.: The Pathological Findings in Four Autopsied Cases of Acromegaly, Monograph 22, Rockefeller Institute for Medical Research, 1927, p. 31, fig. 26. Case of c. v. g. presented as "bull-dog scalp" in an acromegalic person.

It is not our purpose to present here in great detail a review of the earlier literature of the cases in which the condition was due to causes other than pituitary disturbances. This has been well done in the American literature by Stratton,⁶ Madden¹³ and Hammond and Ransom,¹⁴ who presented 2 cases of the inflammatory type. Madden emphasized the fact that the structure of the scalp favors the formation of folds and that abnormal collections of cells, whatever their origin or type, may result in an apparently identical morphologic end result. Hammond and Ransom, in a careful histologic and clinical report of 2 cases of cerebriform nevus of the scalp, stressed the fact that this condition is distinctly different from all other types of *cutis verticis gyrata*. It is apparent therefore, that instead of being satisfied with the clinical-morphologic diagnosis, each case must be studied carefully in an attempt to arrive at a diagnosis based on causation.

There is probably no cutaneous disease which lends itself more readily to immediate clinical diagnosis than *cutis verticis gyrata*. However, this diagnosis should serve only as a provisional working diagnosis on which further intensive study of the case should be based. An accurate history of the circumstances of the onset of the condition may be of value, especially in cases in which the condition is apparently a sequela of trauma, infection (local) or inflammatory disease, in this group the gyri are apt to be less regular in outline and distribution and show evidence of follicular changes, as compared with those in cases in which the condition is due to systemic factors. In dissecting folliculitis of the scalp (*perifolliculitis capitis abscedens et suffodiens*), the appearance of the scalp may after healing present scarring, with the nodules and folds resembling the convolutions of the brain. A history of development of the condition early in life suggests the possibility of nevroid or anomalous developmental etiology, but even in this type of case both study of the local tissue and roentgenographic study of the skull, with special reference to the sellar region, should be carried out.

In all cases in which the cause is not apparent, a biopsy should be performed first as a possible means of detecting specific types of infiltrating tissue, such as leukemia, nevus, tumor and inflammatory cellular elements. When such study fails to indicate the etiologic diagnosis, even in the absence of other gross outward clinical signs, the case should be thoroughly investigated for endocrine disease, including myxedema as well as for pituitary disease involving the anterior lobe. As part of such examination roentgenograms of the skull and of the extremities play an important part. Other important laboratory studies include the basal metabolic test, careful examinations of urine, the test for

13 Madden J. *Minnesota Med* 18:536, 1936.

14 Hammond, G., and Ransom, H. K. Cerebriform Nevus Resembling Cutis Verticis Gyrata, *Arch Surg* 35:309 (Aug) 1937.

diminished sensitiveness to epinephrine and the sugar tolerance test. In the event of failure to identify a definite etiologic factor after thorough investigation, the patient should be kept under observation with periodic reexamination, including repeated roentgen ray examination of the skull, measurement of visual acuity and fields and examination of the urine. It is noteworthy that in both the cases presented here there was evidence of serious metabolic disturbances, although in the second case a relation between the pituitary disease and the metabolic changes ultimately responsible for the patient's death could not be established. The 2 following case reports well illustrate the association of cutis verticis gyrata as a readily detected clinical sign of pituitary disease of the acromegalic type.

REPORT OF CASES

CASE 1.—R. S., a white man aged 44, has been under observation for the past fifteen years with known symptoms of acromegaly. He has had diabetes for five years and urinary incontinence for four years. He has been admitted to the hospital at various times in the last four years on account of pain in the lower part of the back and in the legs, which was diagnosed as sacroiliac arthritis, and sciatica and kyphoscoliosis associated with acromegaly in 1935. In 1937 he was admitted to the hospital with polyuria, polydipsia, loss of weight and muscular weakness of two months' duration. The concentration of sugar in his blood at that time varied from 205 to 230 mg. per hundred cubic centimeters, and his diabetic symptoms were controlled with insulin and diet. In November 1938 he was again admitted on account of pain in the lumbosacral region, for which a laminectomy was performed and from which he made a good recovery. The neurologic examination revealed the following picture: slight bilateral pes cavus; moderate atrophy of all muscular groups of both lower extremities and buttocks; good motor power in the lower extremities, and absence of knee jerks even on reenforcement. The sensory examination showed a saddle-shaped area of analgesia and anesthesia (third, fourth and fifth sacral vertebrae); intact deep sensibility; a band of hyperalgesia anteriorly and posteriorly, just above the iliac crest and extending around the groin and abdomen; loss of sensation of the genitalia, and intact abdominal reflexes bilaterally. Power in the upper extremities was good, but the reflexes were obtained only with reenforcement. The cranial nerves were normal, and the ocular fundi appeared normal. A grossly tested visual field on the left seemed constricted.

Roentgenograms of the spine showed an old osteoarthritic process mainly of the fourth and fifth lumbar vertebrae. The chemical examination of the blood revealed: uric acid 6.6 mg., calcium 12 mg., phosphorus 4 mg., nonprotein nitrogen 33 mg., phosphates 3.2 units and sugar 160 to 260 mg. per hundred cubic centimeters. The blood count showed no abnormality, and the Wassermann and Kahn reactions were negative on repeated examinations. The patient was intelligent and alert, although he walked with some difficulty.

The condition of the scalp had been present for some years, having developed about the same time that the enlargement of his hands and the changes in his facies were noted. After the hair on the scalp was shaved, the entire scalp was found to present deep anteroposterior convolutions, roughly resembling those of the cerebral hemispheres. The forehead also presented deep transverse folds. In

addition to this, physical examination showed striking evidence of an advanced degree of acromegaly. There was general enlargement of the head, thickening of the nose and lips, slight exophthalmos, decided prognathism and enlargement and prominence of the ears. A thickened glabella and prominent malar eminences gave the patient a leonine expression. The teeth were widely spaced, and the palate was high arched. The tongue was rather large, and there were many nevi on the face and trunk. The skin of the face was doughy and inelastic, resembling that in cases of myxedema, and showed an excessive sebaceous secretion. The hair on the scalp was coarse and abundant and concealed the furrows almost



Fig 1 (case 1) —Furrows and folds of the scalp and forehead in a patient with advanced acromegaly (Dr Zeisler)

completely. The chest was barrel shaped and emphysematous. There was kyphoscoliosis of the lower thoracic and lumbar vertebrae, with a protuberance at the lumbosacral junction. The soft parts of the hands were enormously thickened, presenting the characteristic "spade" type of deformity, with sausage-shaped fingers with clubbed ends, thickened skin and localized hyperhidrosis. The feet showed similar changes. The results of physical examination were interpreted as those of advanced acromegaly due to an eosinophilic adenoma of the pituitary, associated with diabetes, osteoarthritis of the vertebral joints and *cutis verticis gyrata*.

Roentgenograms of the skull showed definite enlargement of the accessory sinuses, particularly the frontal, which extended upward to a point almost midway

between the nasion and the vertex. The bones of the calvarium were unusually thick. There was a high degree of calcification of the pineal gland and choroid plexus. There was decided destruction of the structures in the region of the sella turcica, with loss of the floor and posterior clinoid process. The changes were considered typical of those seen in cases of acromegaly.

The bones of the hands were large and the phalanges wide in proportion to their length. There were considerable tufting of the terminal phalanges and hypertrophy of their bases. While these changes are sometimes seen in normal persons, they are more commonly observed in acromegalic changes, namely, that the roentgenographic changes confirmed the clinical diagnosis, namely, that the patient was suffering from a pituitary tumor, with acromegalic changes.

CASE 2.—J. W., a Negro aged 35, was referred to the department of dermatology and syphilology of the Milwaukee County Hospital on Aug. 13, 1929, with

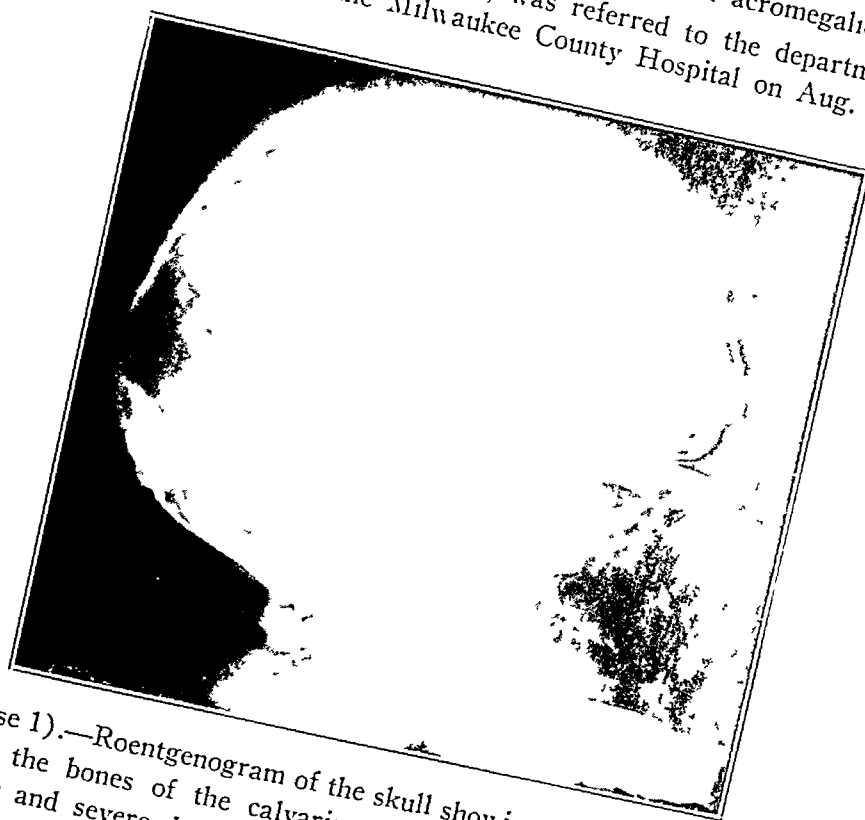


Fig. 2 (case 1).—Roentgenogram of the skull showing enlarged accessory sinuses, thickening of the bones of the calvarium, calcification of the pineal gland and choroid plexus and severe destruction of the structures in the region of the sella turcica, with loss of the floor and posterior clinoid processes.

a provisional diagnosis of cerebrospinal syphilis, which was based on the patient's history that he had been treated for this condition previously in clinics in other cities. Further questioning revealed that his chief complaints were persistent fronto-occipital headache and progressive impairment of vision for ten or twelve years, especially in the left eye, with occasional transient diplopia. There was no history of other symptoms of any description, and he did not recall ever having had lesions suggestive of early syphilis. However, at one of the clinics he had been told that his Wassermann reaction was positive and had received considerable antisyphilitic treatment, without appreciable effect on his symptoms. Questioned as to the duration of the condition of the scalp, the patient stated that it had begun at about the same time the headache and visual symptoms were first noted

and that progression of the symptoms and the changes in the scalp had been of about the same degree. At no time had there been any inflammatory change in the scalp, and he was certain that until twelve or fourteen years preceding his entrance to the hospital his scalp had been perfectly smooth. This statement was corroborated by the patient's wife.

Examination showed the patient to be well nourished but not obese. Mentally he was alert and intelligent, and no evidence of mental aberration could be detected from his conversation. The scalp presented alternate deep furrows and ridges arranged in a gyrate and anteroposterior linear manner and involving the entire

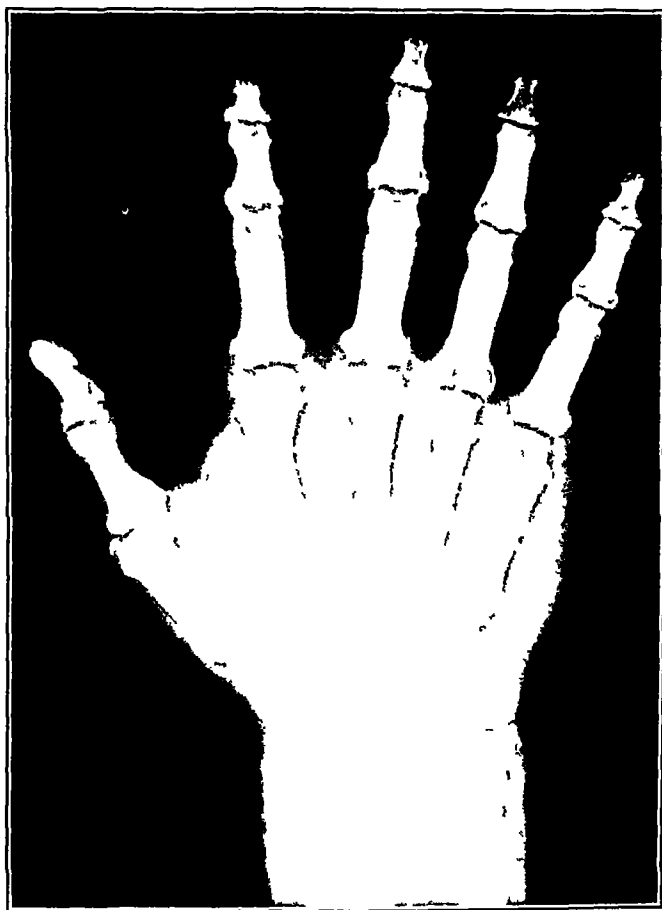


Fig 3 (case 1) —Roentgenographic changes in the hands, showing enormous enlargement of the bones and soft parts, tufting of the terminal phalanges and hypertrophy of their bases

vertex, frontal, parietal and occipital portions of the scalp. The furrows felt rather tightly bound down to the underlying structures, but the ridges were soft and easily movable. The bony landmarks of the face were prominent but not to a greater degree than may occasionally be exhibited by the normal Negro. The skin of the face, especially of the forehead, showed deep wrinkles somewhat suggestive of an earlier stage of the condition present in the scalp. The neurologic examination showed only slight sluggishness of the pupillary reaction to light and weakness of the left external ocular rectus muscle. The tendon reflexes, gait and station

were normal. The extremities were not visibly enlarged. He had no difficulty in wearing gloves or shoes that he had formerly worn. The secondary sex characteristics were normal.

Examination of the eyegrounds showed the retina of the right eye to be pale, and the eyegrounds of the left could not be seen at all owing to active choroiditis; there was practically no vision in the left eye. The visual fields examined subsequently were moderately contracted in the right eye and greatly contracted in the left.

Wassermann reactions of the blood were repeatedly negative. The spinal fluid was normal.

Roentgenograms of the skull showed the bones of the vault to be thick, even for a Negro, with large accessory sinuses and prominent superior maxillas. There was decided thinning of the posterior clinoids, and the anterior clinoid on the left was apparently eroded, with erosion of the floor of the left side into the sphenoid



Fig. 4 (case 2).—Anteroposterior folds over the frontal part of the scalp (Dr. Wieder).

sinus. The metacarpal bones were short and thick. The tubercles of the distal phalanges were particularly prominent, and there were projections extending outward from the bases of the distal phalanges.

During a short period of hospitalization for further study the temperature was continuously normal. The blood pressure averaged 155 systolic and 100 diastolic. The urine showed no sugar at any time. The dextrose tolerance curve was normal. The basal metabolic rate was + 12 per cent. The blood count and the results of chemical examination of the blood were essentially normal (nonprotein nitrogen 37.3 mg., urea nitrogen 27.5 mg., creatinine 1.6 mg. and cholesterol 0.133 mg. per hundred cubic centimeters; sugar 0.8 and sodium chloride 0.462 per cent).

A biopsy was performed. A piece of tissue extending from the crest of a ridge in the vertex to the base of the adjoining furrow was excised. It was cut in a plane transverse to the long axis of the gyrus from which the section was taken, thus enabling comparative study of the hypertrophic center of the gyrus as well as its lateral, bound-down margin. The epidermis showed no remarkable changes.

In the corium the glandular elements and the hair follicles appeared to be unusually well developed, although without definite abnormality. No inflammatory changes were found. The most noticeable deviation from the normal lay in the increased number of the collagen bundles and the intensity of staining in them, especially in the upper half of the corium in the portion of the section corresponding to the crest of the gyrus examined. Although definite formations of fibrous bands could not be identified, the general architecture of the sections was interpreted as being compatible with the theory advanced by Stratton to account for the production of ridges and furrows in *cutis verticis gyrata*, namely, that there may be an inherent tendency for some types of tissue to grow faster than others and that such overgrowth between the dense normal fibrous bands binding the scalp to the pericranium would cause an arrangement of folds, the hypertrophy being chiefly found in the collagen bundles in the case under discussion and in the nevus cells and leukocytes in the various other conditions resembling *cutis verticis gyrata*.



Fig 5 (case 2) —Roentgenogram showing moderately enlarged sella turcica, with thinning of the clinoid processes

In addition to the theory which may account for the mechanism of the development of folds in *cutis verticis gyrata* of acromegalic origin, other explanations must be sought for the occasional case in which the condition is unilateral. Weber¹⁵ cited such a case and stated the belief that in certain persons there exists a difference in "local soil" of corresponding parts of the body, so that a "general agent"—such as a pathologically altered endocrine secretion—exerts a greater effect on one organ than on another and even more on one side of the body than on the corresponding opposite part. No basic explanation of this phenomenon is given.

15 Weber, F. P., and Atkinson, F. R. B. *Brit J Dermat* 40:454, 1928

On the basis of the clinical symptoms, observations on the eyes and the bony changes exhibited in the roentgenograms, a diagnosis of probable eosinophilic tumor of the pituitary gland was made.

The patient was kept under intermittent observation until his death in June 1938. The only therapy of note consisted of a short course of roentgen ray treatments directed to the area of the pituitary in 1931 and 1932; these produced no definite effect on subsequent symptoms, and no remarkable changes were noted in the appearance of the structure of the skull on repeated roentgen ray examination during the succeeding six or seven years.

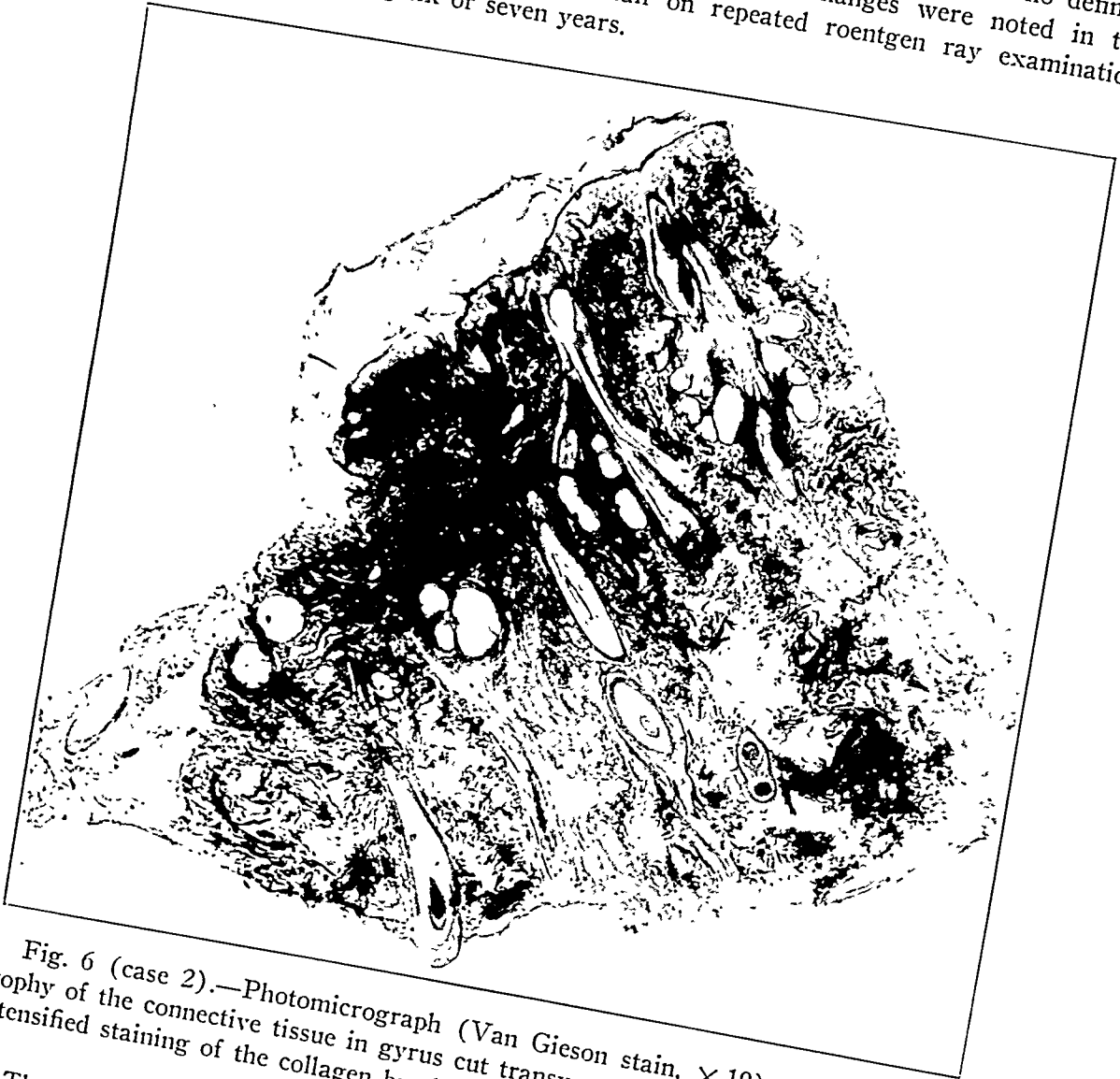


Fig. 6 (case 2).—Photomicrograph (Van Gieson stain, $\times 19$) showing hypertrophy of the connective tissue in gyrus cut transversely and increased number and intensified staining of the collagen bundles in the upper half of the corium.

The patient continued to suffer from severe headaches, chiefly occipital, and the vision was practically unchanged. In October 1937, in the course of a routine check-up re-examination, his blood pressure was found to be 170 systolic and 90 diastolic, and the urine showed numerous hyaline casts and much albumin. His subsequent clinical course during the succeeding eight months was progressively downhill, the patient dying on June 7, 1938, of malignant hypertension with degenerative cardiorenal changes.

The autopsy showed the sella turcica to be widened posteriorly and laterally, measuring 2 cm. anteroposteriorly and 2 cm. laterally. The posterior clinoid

processes were flattened, and the presence or absence of erosion was not noted. The pituitary gland was found to be cystic and enlarged to such an extent that it was difficult to determine the architecture on gross cut sections. On microscopic examination, the capsule was found to be thickened owing to excessive fibrosis. On the surface and occasionally within the body of the gland nests of monocytes and multinucleated cells were found embedded within the connective tissue. The tubular structure of the gland was distorted. The predominating cells were large eosinophils which stained a deep pinkish red with the ordinary hematoxylin-eosin stain. The remaining cells present were few in number. The pars intermedia was occupied by several small cysts containing a colloid-like material. The posterior lobe showed no unusual changes. The microscopic picture was considered compatible with that of chromophilic adenoma of the eosinophilic type, according to the classification of Dott, Bailey and Cushing,¹⁶ which accompanies the hyperpituitary syndrome.

COMMENT

Investigation of the literature together with the 2 additional cases presented here indicates that cutis verticis gyrata may be added to the various other clinical signs pointing to pituitary disease. That it may be almost the only external sign and overlooked as such is shown by the clinical account of case 2. Although only a small proportion of all cases of acromegaly exhibit this finding, it is probable that of the many cases described in the literature, more may have been early signs of oncoming pituitary disease than were recognized as such. Because of this probability, we wish to reemphasize the need for careful study, with the inclusion of routine roentgenographic examination of the skull and extremities in this group of cases. We also wish to emphasize that the finding of a sella normal in size on roentgen ray examination does not necessarily negate the diagnosis of associated cutis verticis gyrata with acromegaly, as illustrated by Sisson's case, which, although one of frank acromegaly, showed a sella of apparently normal size. In some cases a final diagnosis can be established only after prolonged study and repeated reexamination.

Because of the scant attention this subject has been given in the American literature, it is our object to bring our 2 cases of cutis verticis gyrata associated with acromegaly to the attention of other physicians, especially dermatologists, as the latter may be the first to see the patient, and prompt recognition of the significance of the condition may bring about the detection of a serious underlying disease.

Dr S. A. Morton, Columbia Hospital, Milwaukee, interpreted the roentgenograms, and Dr John Grill, Milwaukee County Hospital, Wauwatosa, Wis., supplied the details of the results of autopsy in case 2.

ABSTRACT OF DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: I have recently had the occasion to study histologically 5 cases of cutis verticis gyrata, the specimens from all of which came from a state institution for persons with epilepsy, through Dr. Thomas Butterworth. In none of these were there any symptoms of acromegaly. No nervous disease other than epilepsy could be established in the cases.

I think that it is rather generally granted that cutis verticis gyrata is only a clinical entity. It is doubtlessly not an etiologic entity any more than zoster is. Curiosity naturally centers on what the anatomic explanation for the folds may be. In the histologic studies of the abundant material from the institution, some valuable information came to light. It was emphasized to the surgeon who obtained the biopsy specimens that it was necessary to get the full extent of a convolution, with the sulcus on each side. The result was that some of the slabs of tissue were an inch or two (2.5 to 5 cm.) in length, in fact so long that celloidin (pyroxylin) was employed for embedding. This gave a splendid opportunity for comparing the composition of the different levels of the skin over a long stretch.

One idea as to the reason for these convolutions is that there are fibrous septums extending from the epidermis to the periosteum underneath, that they bind the skin more closely at those points—comparable to Cooper's ligaments in the breast, which are responsible for the pigskin markings in mammary cancer—and that there are increases of fibrous tissue between these points of attachment which cause a bulging of the skin (convolution) of the scalp. Such phenomena did not appear in any of my sections. What little increase in tissue there was in the bulges appeared to be due to fat.

In my sections, the factor that seemed to be the more responsible for the bulge was the hair shafts. I noted that Dr. Zeisler remarked in his first case that the hairs were numerous and were robust, and I think that it is probably a matter of common clinical observation in epileptics that the hair is commonly robust and closely placed. From the preliminary study of my sections, too, it would appear that the hair shafts are both more robust and more closely placed than they are in normal scalps. In addition, a good sized slab of this scalp tissue—for example, $\frac{1}{8}$ or $\frac{1}{4}$ inch (0.3 or 0.6 cm.) thick and 2 inches (5 cm.) long—was cleared by the wintergreen oil technic (Spalteholz). The skin became so transparent that the individual hair shafts (black) stood out. By transmitted light, on examining with the naked eye, one could then recognize the abundance of the hair shafts.

After this, it is logical to try to reconcile this abnormal growth of hair with endocrine, nervous conditions, in which the pituitary comes under consideration at once. In short, at least tentatively, it is permissible to regard the growth processes of hair, whether initiated by pituitarism or not, as the possible explanation of the increased bulk of tissue in the scalp. With this increased bulk the scalp buckles and results in convolutions.

DR. ERWIN P. ZEISLER, Chicago: I hope that none of the American dermatologists will feel particularly slighted because their names were not mentioned in this article. Dr. Wise, I think, recorded the first American case of this condition; Dr. Oliver also reported a case some time ago, and there have been several others. But most of these reports were clinical descriptions of the disease, and no cause was recorded. I think in 1 case syphilis was mentioned as a possible etiologic factor. In fact, in many of the earlier descriptions of the disease it was stated that the condition may be simply a developmental anomaly or a nevus.

I have not said anything about the possible treatment of this condition. It is obvious that nothing can be done for it except in the cerebriform nevi. Such lesions have been removed surgically, with subsequent plastic procedure and good cosmetic results.

I think that in many of the cases in which the condition was recorded as due to inflammatory changes and trauma the presenters have failed to recognize the possible endocrine basis. Cases are reported in which the condition is called impetigo or psoriasis of the scalp followed by cutis verticis gyrata. It is nonsense to suppose that a simple inflammatory change without some serious metabolic disturbance could produce gyri and furrows that look like cerebral hemispheres. I think that the same argument applies against trauma as a cause.

I suspect that in the future all dermatologists will probably make more careful studies with reference to the pituitary cause of this disease.

PITYRIASIS-ROSEA-LIKE DERMATITIS FOLLOWING GOLD THERAPY

REPORT OF TWO CASES

UDO J. WILE, M.D.

Professor of Dermatology and Syphilology
AND

CHARLES J. COURVILLE, M.D.

Instructor in Dermatology and Syphilology
ANN ARBOR, MICH.

Chrysotherapy has been employed with encouraging results in the constitutional treatment of arthritis, lupus erythematosus and various forms of tuberculosis for the past twenty-five or more years. However, the use of gold has been attended in many instances by accidents of varying degrees of severity. Dermatitis has been a frequent manifestation of toxicity. Recent observation of 2 unusual cases in which there were eruptions similar to pityriasis rosea accompanied by lesions on the mucous membranes appearing during gold therapy has stimulated our interest in this subject.

Gold was first used therapeutically in 1810 by Chrestien for the treatment of pulmonary tuberculosis.¹ Koch showed that the presence of gold was lethal to the tubercle bacillus in vitro in 1890. This apparently stimulated others to further investigation for suitable therapeutic forms of gold and their effect on various diseases. Bruck and Glück² were the first in recent years to attempt treatment of tuberculosis by gold, using a potassium gold cyanide compound in cases of lupus vulgaris. Speiss and Feldt³ separately and together reported the use of various gold compounds in tuberculosis between 1912 and 1916. In 1917 Feldt synthesized the compound "krysolgan," which has since been used in Germany and elsewhere for many years in the treatment of

Studies and contributions from the Department of Dermatology and Syphilology, University of Michigan Medical School, service of Dr. Udo J. Wile.

1. Cited by Franklin, J. L.: Treatment of Lupus Erythematosus with Sano-crysin, Brit. J. Dermat. **46**:66 (Feb.) 1934.

2. Bruck, C., and Glück, A.: Ueber die Wirkung von intravenösen Infusionen mit Aurium-Kalium cynatum (Merck) bei äusserer Tuberkulose und Lues, München. med. Wchnschr. **60**:57, 1913; abstracted, J. Cutan. Dis. **31**:1058, 1913.

3. Cited by Schamberg and Wright.⁶

cutaneous and other forms of tuberculosis Ruete,⁴ in 1913, used a gold and potassium cyanide compound for the treatment of lupus erythematosus, and Martenstein⁵ followed in 1922, reporting on a rather extensive series of patients with lupus erythematosus treated by the gold thiophenol compound (krysolgan) produced by Feldt Schamberg and Wright⁶ introduced into this country gold therapy of lupus erythematosus Much of the present knowledge concerning the pharmacology and therapeutics of gold is owed to Mollgaard,⁷ who reported in 1924 the use of "sanocrysin" (gold and sodium thiosulfate) for the treatment of pulmonary tuberculosis Feldt⁸ used gold experimentally in the treatment of arthritis in 1926 Later it was employed in a large number of cases by Forrester,⁹ Hartfall and Garland,¹⁰ Bach,¹¹ Pemberton¹² and many others

Nearly all of the writers cited have reported along with their results of gold therapy various toxic reactions which occurred during the course of treatment The incidence of toxic reactions has varied with different observers Copeman and Tegner¹³ stated that the importance of accidents has been overemphasized Mayer¹⁴ found reactions in 10 per cent of 1,400 patients with tuberculosis treated with gold, these

4 Ruete, A Ueber den Wert des Aurium-Kalium cyanatum bei der Behandlung des Lupus vulgaris und Erythematodes, Deutsche med Wchnschr **36** 1727 (Sept 4) 1913

5 Martenstein, H Die Behandlung des Lupus erythematodes mit Krysolgan, Klin Wchnschr **1** 2235 (Nov 4) 1922

6 Schamberg, J F, and Wright, C Use of Gold and Sodium Thiosulfate in the Treatment of Lupus Erythematosus, Arch Dermat & Syph **15**:119 (Feb) 1927

7 Mollgaard, H Chemotherapy of Tuberculosis, Copenhagen, A Busck, 1924, The Theoretical Basis for the Sanocrysin Treatment of Tuberculosis, Brit M J **1** 643 (April 4) 1925

8 Cited by Copeman and Tegner¹³

9 Forrester, J Treatment of Rheumatoid Arthritis with Gold Salt Injection, Lancet **1** 441 (Feb 27) 1932

10 Hartfall, S J, and Garland, H G Gold Treatment of Rheumatoid Arthritis, Lancet **2** 8 (July 6) 1935, Reactions Following Gold Injections, Brit M J **1** 276 (Feb 9) 1935, Further Observations on Gold Treatment of Rheumatoid Arthritis, Lancet **1** 1459 (June 27) 1936 Hartfall, S J, Garland, H G, and Goldie, W Gold Treatment of Arthritis Review of Nine Hundred Cases, ibid **2** 184 (Oct 2), 838 (Oct 9) 1937

11 Bach, F Gold in the Treatment of the Rheumatic Diseases, St Barth Hosp J **43** 206 (Aug) 1936

12 Pemberton, H S One Hundred Cases of Chronic Arthritis Treated with Gold, Lancet **1** 1037 (May 4) 1935

13 Copeman, W S C, and Tegner, W Review of Gold Therapy, Lancet **1** 554 (March 6) 1937

14 Mayer, C Gold Treatment of Pulmonary Tuberculosis, Brit J Tuberc **28** 131 (July) 1934

were mild for the most part. Crosby¹⁵ stated that accidents are of high incidence in spite of care and felt that they have been "glossed over" in reports. Towle,¹⁶ in reviewing the results of gold therapy in 266 cases of lupus erythematosus in America, noted untoward reactions in 41.9 per cent. Hartfall and Garland¹⁰ noted toxic reactions in 41.9 per cent of 900 cases of arthritis, and in 35.3 per cent the reactions were so serious that therapy was stopped.

The accidents occurring during gold therapy have been described by several observers.¹⁷ In general, the reactions have been classified as follows: local, at the site of injection; focal, at the seat of the inflammatory process, and general, or systemic. The last group includes the immediate reactions, such as malaise, pyrexia and gastrointestinal disturbance. Albuminuria has occurred fairly frequently. There have been instances of involvement of the central and peripheral nervous systems. Reactions in the bone marrow, as evidenced by purpura and aplastic anemia, have often been described and frequently have terminated fatally. Dermatitis has been a frequent observation.

The relative incidence of reactions involving the skin and mucous membranes compared to other types of reactions has been high, according to most observers. Hartfall and Garland¹⁰ found that 69 per cent of all patients with toxic manifestations had cutaneous reactions alone or in association with others. The majority of cutaneous reactions developed during treatment, but in 21 per cent they appeared from one to twelve weeks after treatment had been discontinued. The cutaneous reactions in general resemble those associated with other heavy metals, such as arsenic, bismuth and mercury. Pruritus, generalized or localized, has been noted by many observers. This may be severe and associated with erythema which may progress to exfoliative dermatitis which has terminated fatally in some instances, but recovery is the rule. Morbilliform and scarlatiniform eruptions are relatively common, as well as papular and papulosquamous lesions. The dermatitis sometimes becomes eczematous. Vesicular and bullous lesions have been described in some cases as appearing similar to herpes simplex or zoster. Hyperkeratoses have been observed as late sequelae.

Lesions of the mucous membranes have been described on many occasions. Metallic taste in the mouth is noted occasionally as a warning

15. Crosby, G. J. V.: Accidents of Gold Treatment of Rheumatoid Arthritis, *Lancet* 1:1463 (June 27) 1936.

16. Towle, H. P.: The Present Status of Gold Therapy, *New England J. Med.* 204:487 (March 5) 1937.

17. Driver, J. R., and Weller, J. N.: Untoward Results from the Use of Gold Compounds, *Arch. Dermat. & Syph.* 23:87 (Jan.) 1931. Pemberton.¹²

of more serious damage. Loss of sensation of taste for a period of time has been reported¹⁸. Congestion of the fauces and redness of the buccal mucosa have been observed, and these have progressed to erosive and ulcerative stomatitis which has been severe enough to interfere seriously with nutrition. In addition, ulcerative gingivitis and pharyngitis have caused dysphagia in some cases. Involvement of the conjunctiva and cornea have been mentioned by some observers alone and in association with other findings. Ketron¹⁹ described a patient treated by gold and sodium thiosulfate for lupus erythematosus in whom bullous erythema multiforme developed with stomatitis, conjunctivitis and keratitis which went on to corneal scarring and permanent blindness.

Cutaneous lesions of rather unusual types have been reported. Moore¹⁸ observed shining particles of gold on the volar surfaces of the finger tips of a patient seven minutes after an intramuscular injection of aurothiodextrose on two occasions. Throne, Kingsbury and Meyers²⁰ reported 2 cases in which lesions developed that were identical with lichen spinulosus during gold therapy. Pillsbury and Kulchar²¹ presented 2 patients with vitiligo in whom after they received gold and sodium thiosulfate a prolonged dry scaling erythematous eruption developed only on depigmented areas of the body. Roche²² mentioned a patient in whom giant urticaria developed. Schamberg²³ cited a case in which a solution of colloidal gold had accidentally been injected outside the vein, with a resultant greenish blue discoloration which persisted for at least six months. Boon²⁴ reported a case of alopecia, stomatitis and exfoliation of the nails. Mayer¹⁴ stated that in 2 per cent of 1,400 patients treated with gold and sodium thiosulfate for tuberculosis lilac blue pigmentation developed limited to the exposed areas or areas exposed to ultraviolet rays. This pigmentation persisted for a long time

18 Moore, T. Reactions Following Gold Injections, *Brit M J* **1** 389 (Feb 3) 1935

19 Ketron, in discussion on Munson. Lupus Erythematosus, *Arch Dermat. & Syph* **17** 742 (May) 1928

20 Throne, B., Kingsbury, J., and Meyers, C. N. Unusual Clinical Manifestations Following Intravenous Administrations of Gold Compounds, *Arch Dermat. & Syph* **25** 494 (March) 1932

21 Pillsbury, D. M., and Kulchar, G. V. Gold Dermatitis Limited to Depigmented Skin, *Arch Dermat. & Syph* **27** 36 (Jan) 1933

22 Roche, H. Precautions in Sanocrysin Therapy, *Brit M J* **1** 31 (Jan 4) 1936

23 Schamberg, J. F. Chrysoderma, *Arch Dermat. & Syph* **18** 862 (Dec) 1928

24 Boon, T. H. Complications of Gold Therapy, *Brit M J* **1** 780 (April 9) 1938

but ultimately disappeared. Reactions of the skin similar to lichen planus have been reported by Pautrier and Roederer²⁵ and by Milian.²⁶

We were able to find only 3 cases in which lesions similar to pityriasis rosea followed gold therapy. Simons²⁷ merely mentioned that in a patient with lupus erythematosus treated with gold an eruption developed which was similar to pityriasis rosea. Kiess²⁸ reported a pityriasis-rosea-like eruption occurring in a 33 year old woman after she received 1.6 Gm. of aurophos for lupus vulgaris. Rattner²⁹ stated that he saw an eruption resembling pityriasis rosea in a patient following gold treatment for lupus erythematosus.

During the past eight months we have encountered 6 cases of dermatitis of various types which we have attributed to gold therapy. In 2 of these cases the eruptions have been similar to pityriasis rosea, and because this manifestation is so unusual we have felt it worth while to draw attention to them.

REPORT OF CASES

CASE. 1.—L. C., a 46 year old English housewife, had been treated at the Rackham arthritis unit of the University of Michigan Medical School for the past year for atrophic arthritis of eight years' duration. Her past history revealed fair general health and occasional attacks of urticaria.

On Aug. 24, 1939 intramuscular gold therapy was started with myochrysin (gold sodium thiomalate), which was given weekly, the dose beginning with 10 mg. and increasing each week until 100 mg. was given in the fifth injection. This dosage was maintained for thirteen weeks, at which time she had received a total of 1,010 mg. of the drug. A few minutes after having received the twelfth injection redness of the conjunctiva, flushing of the face, perspiration of the brow, faintness and apprehension developed. This was followed by a burning sensation in the eyes, which persisted for three days. Two weeks after the final injection she began to complain of sore mouth. Two weeks later she noted a pruritic scaling eruption of the scalp, and the following week a fairly generalized rash involving mainly the shoulders and trunk appeared.

Shortly after this, she was seen in the dermatologic clinic, where examination revealed a widespread, only slightly inflammatory, dry, scaling, patchy eruption of the scalp. Confined to the trunk was a mildly erythematous eruption, composed of papulosquamous lesions with fine scales, which was most evident in the midline

25. Pautrier, L. M., and Roederer, J.: Aurides lichéniennes verruqueuses en nodules isolés et en placards, végétants, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **45**:139 (Feb.) 1938.

26. Milian, G.: Le lichen plan aurique, Bull. Soc. franç. de dermat. et syph. **[46]**:38 (Jan.) 1939. Schneidewind, A.; Albertal, M., and Trajtenberg, S.: Crisiasis, Rev. Assoc. méd. argent. **52**:792 (Aug. 15) 1938.

27. Simons, R.: Twenty-Five Years of Gold Treatment of Lupus Erythematosus, Brit. J. Dermat. **50**:575 (Nov.) 1938.

28. Kiess, O.: Ueber eine der Pityriasis rosea "ähnliche unter Pigmentierung abheilende Gold-(Aurophos-) Dermatitis, Dermat. Wchnschr. **86**:133 (Jan. 28) 1928.

29. Rattner, H.: Personal communication to the authors.

posteriorly and tended to sweep around in the lines of cleavage. This eruption was similar to pityriasis rosea. No primary plaque was present. There was a mild hyperkeratosis of the right palm and an erythematous plaque on the left palm. The lower extremities were spared. The breath had a metallic odor, and there were several superficial erosions on the buccal mucous membrane and on the lower lip.

Three weeks later on reexamination considerable loss of hair from the scalp was noted. There were postauricular erythema and scaling. The mouth remained about the same. The eruption on the trunk had spread to involve the upper portions of the extremities.

On March 17, 1940 she was presented at the joint meeting of the Chicago and Detroit dermatologic societies in Ann Arbor.³⁰ Examination at this time revealed a greasy scaling eruption of the scalp with postauricular extension, erythema about the eyes and periumbilical erythema and scaling. The same scaling maculopapular lesions were noted on the back, but in the axillas there were elongated scaly,

Results of Studies of the Blood

Date	Blood Cells per Cu Mm		Hemo globin, per Cent	Differential Count, in per Cent				
	Red	White		Poly- morpho nuclear Leuko- cytes	Baso- phils	Posino phils	Lympho- cytes	Mono nuclear Leuko- cytes
8/ 1/39*	3,400,000	5,000	76	70	0	3	25	2
10/11/39	4,450,000	3,600	77	80	0	4	13	3
11/18/39 †		3,500	74					
11/25/39		4,800	75					
1/ 4/40 ‡		4,450	80	77	0	2	18	3
5/31/40		4,500	78					

* Before gold was administered

† At the time of first symptom of intolerance of gold

‡ At the time of first examination following onset of reaction

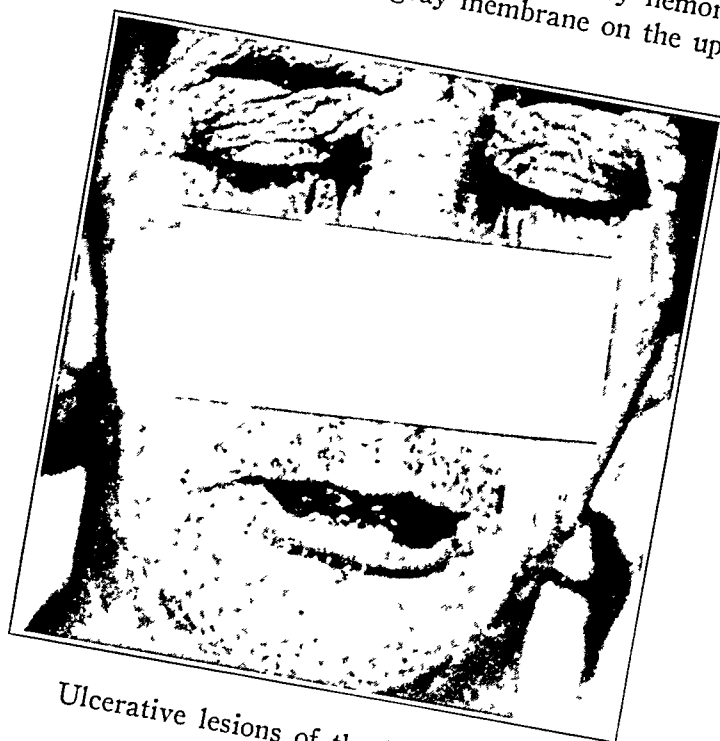
crinkled, stria-like lesions. There was a patch of lichenoid papules on the anterior surface of the left wrist. The lesions of the mucous membranes were about the same as previously noted.

On May 31 she was again examined. At this time no lesions of the mouth were noted. The eruption on the body had subsided, leaving residual pigmentation and slight atrophy at the sites of previous lesions.

Laboratory Data—The Kahn reaction of the blood was negative. The urine was normal throughout the period of observation.

CASE 2—O L, a 54 year old white farmer, was being treated at the Rackham arthritis unit of the University of Michigan Medical School for chronic active atrophic arthritis. On August 18, 1939 intramuscular gold therapy with myochrysin was instituted. He received injections beginning with 10 mg, gradually increasing to 100 mg and continuing with this dosage. On October 16, after having received 630 mg, he complained of moderate pruritus of the legs, this was not made worse by further treatment. On November 25, at which time he had received a total of 1,230 mg, he complained of a severe generalized pruritic dermatitis, swelling of the eyelids and sore mouth. Injections were discontinued at this time.

Two weeks later he was examined in the dermatologic clinic and presented a slightly erythematous papulosquamous eruption on the trunk and proximal portions of the extremities. The characteristic lesions were round or oval, slightly elevated, discrete and covered by a branny type of scale. On the chest and back the lesions followed the lines of cleavage. There was no evidence of a herald plaque. Many of the lesions had been excoriated and were covered by hemorrhagic crusts. The face was erythematous. There was a gray membrane on the upper lip. The lower



Ulcerative lesions of the lips (case 2).

Blood Studies

Date	Blood Cells per Cu. Mm.		Hemo- globin, per Cent	Poly- morpho- nuclear Leuko- cytes	Differential Count, in per Cent			
	Red	White			Baso- phils	Eosino- phils	Lympho- cytes	Mono- nuclear Leuko- cytes
8/15/39 *								
10/16/39 †	4,100,000	9,800	79	69	0	1	26	4
10/24/39	3,700,000	6,400	82
12/11/39 ‡	4,930,000	8,400	84	75	0	1	16	8
		8,500	85					

* Before gold was administered.

† At time of first complaint of pruritus.

‡ Seventeen days after onset of severe pruritus.

lip was covered by a yellowish brown crust, and there were many fissures, especially at the angles of the mouth. The eyelids were erythematous and edematous and were covered by a branny type of scale. There were crusting of the margins of the lids and mild hyperemia of the conjunctivas.

With bland topical treatment and intravenous injections of sodium thiosulfate the symptoms sufficiently improved to warrant the patient's discharge from the hospital in ten days. He stated in a letter one month later that his eruption had entirely disappeared.

Laboratory Data.—The Kahn reaction of the blood was negative. The urine was normal throughout the period of observation except for a few white blood cells.

COMMENT

The question might be raised as to whether or not the condition in these cases was latent or incubating pityriasis rosea made manifest clinically by the stimulation of injections of a gold compound. The following facts point against this concept. There was no initial lesion or plaque, the lesions of the mucous membranes were a definite part of the picture and are rarely, if ever, seen in pityriasis rosea, and there were pruritus and scaling of the scalp, with diffuse alopecia and palmar lesions in 1 case.

We felt that these patients presented cutaneous reactions due to intolerance to gold used therapeutically. If this is true, the accidents may be due either to overdosage or to individual hypersensitivity to the drug. Furthermore, we are unable to suggest any certain means of prevention or foretelling the occurrence of toxic reactions. The fact that the reaction occurred two weeks after the last injection in 1 case suggests that there is a cumulative action and warns against the use of large doses. Frequent urinalysis was no help in predicting these accidents. It is, however, important because of the possibility of renal involvement. The white blood count was significantly lowered in 1 of the cases, and undoubtedly the blood picture should be followed in all patients receiving gold to avoid depression of the bone marrow. The sedimentation rate is probably of little value as a prognostic aid in gold intolerance, since it is lowered if the course of the infectious process is favorable. Several writers, including Wilson,³¹ have advised the use of calcium with gold to prevent the occurrence of untoward sequelae. This has not been tried here. The administration of large doses of vitamins A, B and C as a prophylactic measure was suggested by Secher.³² Undoubtedly gold should not be used when the disease process is acute.

SUMMARY

Reports on 2 patients are presented, in whom lesions of the mucous membranes and a dermatitis similar to pityriasis rosea developed while they were receiving intramuscular injections of myochrysin for arthritis.

Most of the recent literature on cutaneous reactions to gold is briefly reviewed.

Dr Richard Freyberg, of the Rackham Arthritis Unit, cooperated in this study.

31 Wilson, J. Prophylaxis of Severe Reactions in Gold Salt Therapy, *Tubercle* 18: 168 (Jan.) 1937.

32 Secher, K. Prevention of Complications During Gold Therapy of Tuberculosis and Arthritis, *Lancet* 1: 996 (April 30) 1938.

HEREDITARY EDEMA OF THE LEGS
(MILROY'S DISEASE)
ASSOCIATED WITH OTHER CONGENITAL ANOMALIES

WILLIAM A. ROSENBERG, M.D.
CHICAGO

A case of hereditary edema of the legs with other congenital anomalies recently came under my observation. Hereditary edema of the legs being rare, its combination with other congenital anomalies warrants reporting this case as one of unusual interest.

REPORT OF A CASE

L. L., a white woman aged 28, was first seen at the Northwestern University Medical School on April 15, 1939. She stated that her limbs had been enlarged since infancy and that her mother and an aunt had the same condition. The enlargement appeared soon after her birth and gradually progressed during her growth and development. She had experienced no discomfort until about one and one-half years before her appearance at the clinic, when painful swelling of both feet developed, more evident during the afternoon and evening. Rest at night, however, did not materially reduce the swelling or relieve the pain. Properly fitted shoes were prescribed and worn, and as a result the painful edema practically disappeared. The original enlargement of the limbs, however, persisted.

Examination revealed a well nourished, intelligent woman, 5 feet and 3 inches (160 cm.) in height, weighing 184 pounds (83.5 Kg.) and having slightly dry but otherwise normal skin. The hair of the scalp was fine, scant and blond so that the scalp could easily be seen through the sparse growth, particularly over the vertex, a condition which had been present since childhood. The head was normal in contour. The left eye was blind and had been since infancy; it showed a slight strabismus, for which an operation had been performed when she was 11 or 12 years old. She stated that her teeth had come in crooked and far apart. The upper teeth had been extracted because of poor condition. The lower incisor and canine deciduous teeth had fallen out and had never been replaced. The two upper first deciduous incisors had remained as baby teeth until extracted.

The heart and lungs were normal. Her blood pressure was 120 systolic and 60 diastolic. The abdominal, gastrointestinal and genitourinary examinations gave essentially negative results. The hands were puffy and cold. The lower extremities were thickened from the knees down, the circumference being 12 inches (30.5

From the Department of Dermatology and Syphilology, Northwestern University Medical School, Arthur W. Stillians, M.D., Director.

cm) at the ankle and 17 inches (43 cm) at the calf. The skin over the thickened limbs was normal, with no pitting on pressure. The left foot had six toes.

The urine was normal. A blood count showed 80 per cent hemoglobin and 3,890,000 erythrocytes and 10,690 leukocytes per cubic millimeter, with a normal differential count. The basal metabolic rate was —13 per cent. The Wassermann reaction of the blood was negative. Chemical analysis of the blood showed 116.9 mg of sugar, 10.8 mg of calcium, 35.3 mg of phosphorus and 494 mg of chlorides per hundred cubic centimeters. The carbon dioxide-combining power was 37.9 cc per hundred cubic centimeters.

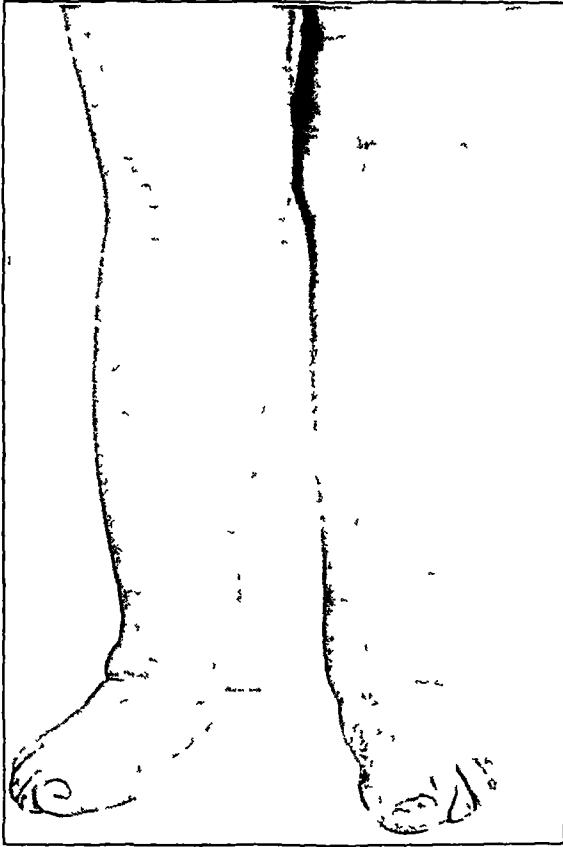


Fig 1—Symmetric thickening from the knees down

Roentgenograms of the feet revealed no abnormality of the right foot but showed two proximal phalanges articulated with the second metatarsal bone on the left foot. The sella turcica was round and within normal limits as to size. It measured 12 mm in its longest diameter. There was no evidence of a skeletal anomaly of either hand.

CLINICAL FEATURES

Special Features—The unusual features in this case not previously reported were retention of the deciduous teeth, six toes on the left foot, congenital strabismus with amblyopia of the left eye and dystrophy of the hair. Other concurrent features, such as hydrocele, have been reported.

by Boks¹ and by van Vliet.² Faber and Lusignan³ reported a case of hereditary elephantiasis with a hydrocele and spina bifida occulta.

Description.—The disease consists of enlargement of the soft tissues of one or more extremities, usually the lower, associated with firm edema of the affected parts. The enlargement is due mainly to compression and hypertrophy of the connective tissue and to the presence of numerous dilated channels in the cutis. Roentgen examinations show no thickening of the bones. A hereditary element is present in the majority of cases. In the family reported by Milroy⁴ the disease occurred in six

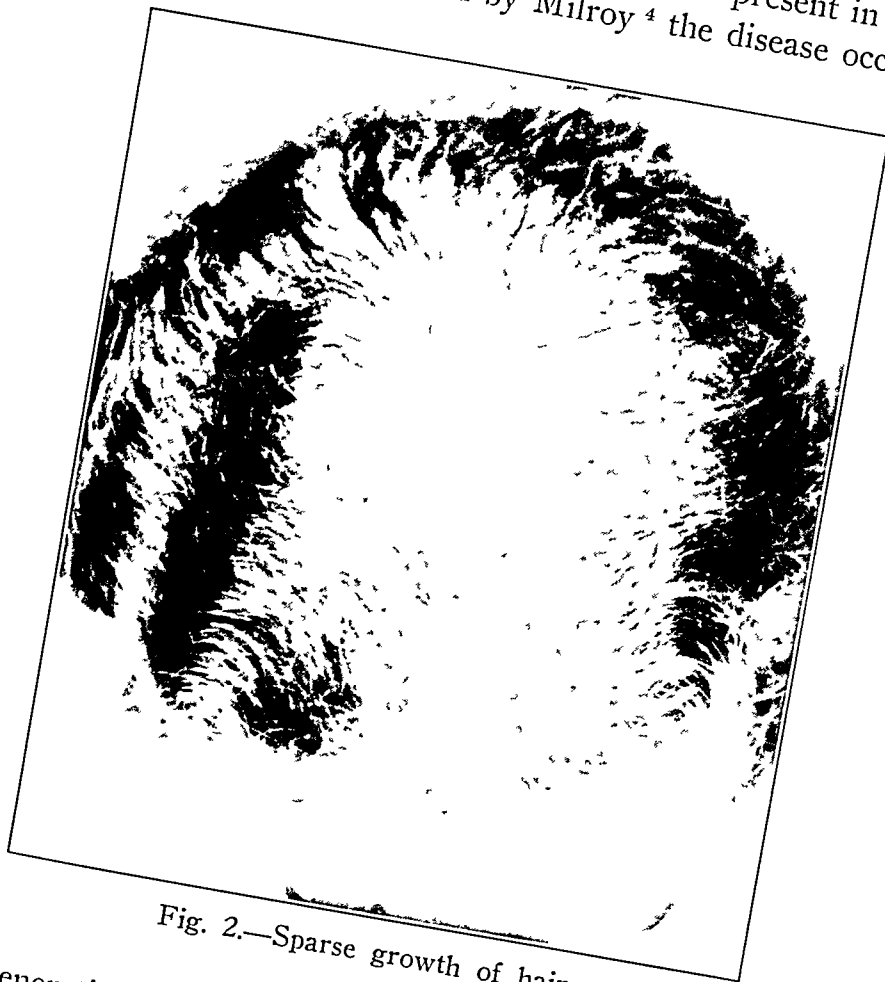


Fig. 2.—Sparse growth of hair.

successive generations. The cases fall into two groups: those in which swelling is present at birth and those in which it may occur in childhood, at puberty or even during early adult life.

1. Boks, D. B.: Congenital Familial Edema of the Lower Extremities, *Nederl. tijdschr. v. geneesk.* **1**:416, 1913.
2. van Vliet, J. C.: Congenital Edema of the Lower Extremities in One Family, *Nederl. tijdschr. v. geneesk.* **2**:1092, 1913.
3. Faber, H. K., and Lusignan, H. R.: Hereditary Elephantiasis, *Am. J. Dis. Child.* **46**:816 (Oct.) 1933.
4. Milroy, F. W.: Chronic Hereditary Edema, *J. A. M. A.* **91**:1172 (Oct. 20) 1928.

Acute Attacks—An unusual feature of the disease consists of acute attacks of chills and fever, with hyperemia, edema, swelling and pain of the affected extremities. The condition during these attacks sometimes resembles erysipelas and occasionally is described as lymphangitis. The attacks were first noted by Meige⁵. Later they were noted by Hope and French⁶ in many of their series, by Hamman⁷ and by Brandt⁸ in 5 of his 13 cases. Acute attacks have been chiefly confined to cases in which the characteristic swelling of the extremities has appeared some time after birth.

HISTORICAL REVIEW

Milroy⁹ in 1892 described in detail 22 cases occurring in six generations of a family consisting of 97 persons. The condition is frequently called Milroy's disease in this country. Meige⁵ in 1898 reported 8 cases in four generations of a family. The disease is frequently referred to as Meige's disease in France. Similar cases were reported by Hille¹⁰ in 1841. Nonne¹¹ in 1890 reported 4 cases of elephantiasis congenita hereditaria in one family and stated that he could find no previous report of similar cases. Desnos¹² in 1891 also indicated the possibility of heredity as a cause of edema when he reported a case and remarked that the condition was more frequent in females and, from a hereditary point of view, more often found in the maternal line. Griffith and Newcomet¹³ reported a case of a condition that they regarded as allied in some respect to Milroy's disease, a child, aged 4 years, had edema of the face and of the left leg which developed at 3 months of age. Weber and Schluter¹⁴ recorded late onset in 2 sisters, the condition beginning when they were 20 and 22. Hope and French⁶ also described

5 Meige, H. *Dystrophie oedemateuse héréditaire*, Presse méd. 2 341, 1898.

6 Hope, W. B., and French, H. *Persistent Hereditary Oedema of the Legs*, Quart. J. Med. 1 312, 1908.

7 Hamman, L. *Milroy's Disease*, M. Clin. North America 1 182, 1917.

8 Brandt, G. *Ueber familiäre Elephantiasis cruris*, Mitt. a. d. Grenzgeb. d. Med. u. Chir. 37 56, 1923.

9 Milroy, F. W. *An Undescribed Variety of Hereditary Edema*, New York M. J. 56 505, 1892.

10 Hille, J. *Ueber die Elephantiasis*, Wchnschr. f. d. ges. Heilk., 1841, pp. 433 and 457, cited by Brandt⁸.

11 Nonne, M. *Vier Fälle von Elephantiasis congenita hereditaria*, Virchows Arch. f. path. Anat. 125 189, 1890.

12 Desnos. *Oedème rhumatismal chronique*, Bull. et mém. Soc. méd. d. hôp. de Paris 3 65-73, 1891.

13 Griffith, J. P. C., and Newcomet, W. S. *Types of Oedema in Infancy and Childhood*, Tr. A. Am. Physicians 12 399, 1897.

14 Weber, F. P., and Schluter, A. *Nonne-Milroy-Meige Oedema, of Late Onset, in Sisters*, Proc. Roy. Soc. Med. 30 933, 1937.

a case of the disease in a child aged 3 months, and Lannois¹⁵ reported a case in which the patient was 14 months of age. Debove¹⁶ in 1902 reported a case of segmentary edema in a woman aged 25 who had suffered from swelling of the lower part of the left leg since the age of 8 years. The swelling was not uniform but was limited to segments of the foot, leg and thigh.

PATHOLOGY AND PATHOGENESIS

Among the hypotheses that have been advanced is the theory of Meige,¹⁷ who stated the belief that there is a congenital malformation of the trophic centers in the spinal cord regulating the growth of cellular tissue. Rapin¹⁸ postulated an embryonic dyscrasia of the mesoblast. Valobra¹⁹ implicated the nervous center controlling the secretion of lymph. Spiller²⁰ speculated on the role played by the vasomotor nerves in the causation of the edema, while some authors attributed the condition to endocrinopathy.

Microscopic examination of the affected part of the leg has been made only a few times. Stoesser²¹ stated that there is a fibrosis in the subcutaneous tissue. Sussini and Casaubón²² gave a more detailed description. They noted that the epidermis is apparently redundant. The cutis consists of dense fasciculated connective tissue containing islands and foci of cells, the latter often perivascular. The panniculus is segmented by dense layers of fibrous tissue. Elterich and Yount²³ in their case noted extensive fibrosis replacing the subcutaneous tissue.

15. Lannois, M.: Une observation de trophœdème chronique héréditaire, *Nouv. iconog. de la Salpêtrière* **13**:631, 1900; *Hereditary Chronic Oedema of the Lower Limbs*, M. Rev. **4**:99, 1901.
16. Debove: Oedème segmentaire des membres inférieurs, *Bull. et mém. Soc. méd. d. hôp. de Paris* **14**:1172, 1897.
17. Meige, H.: Le trophœdème chronique héréditaire, *Nouv. iconog. de la Salpêtrière* **12**:453, 1899.
18. Rapin, E.: Sur une forme d'hypertrophie des membres, *Nouv. iconog. de la Salpêtrière* **14**:472, 1901.
19. Valobra, I.: Les oedèmes circonscrits aigus et chroniques sous la dépendance du système nerveux (rôle de la sécrétion lymphatique dans leur pathogénie), *Nouv. iconog. de la Salpêtrière* **18**:201 and 255, 1905.
20. Spiller, cited by Ayala, G.: Le trophœdème chronique et le système endocrinosympathique, *Encéphale* **1**:319, 1913.
21. Stoesser, A. V.: The Hypertrophies of Infancy and Childhood, *Am. J. Dis. Child.* **35**:885 (May) 1928.
22. Sussini, M., and Casaubón, A.: Trofoedema crónico de Meige: Resultados quirúrgicos, *Rev. de especialid.* **1**:474, 1926.
23. Elterich, T., and Yount, C. C.: Congenital Elephantiasis, *Am. J. Dis. Child.* **29**:59 (Jan.) 1925.



Fig 3—Lower incisors and canine deciduous teeth had fallen out and had never been replaced

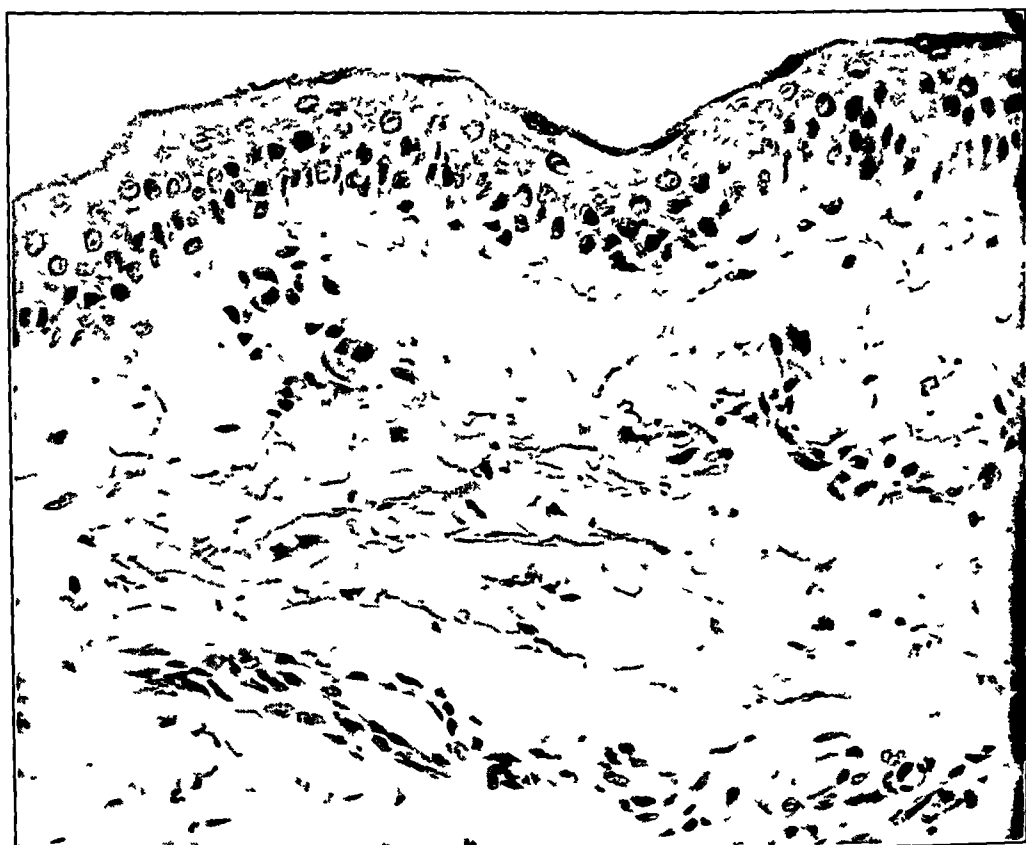


Fig 4—Photomicrograph showing elastic tissue fibers ($\times 325$)

Throughout these sections there was a mononuclear perivascular exudate in the affected fatty tissue. McGuire and Zeek²⁴ studied sections of the skin from 2 patients. The epidermis in 1 case was normal and in the other slightly thickened; the corium, and especially the hypoderm, showed severe edema in which pools of fluid were present in spaces

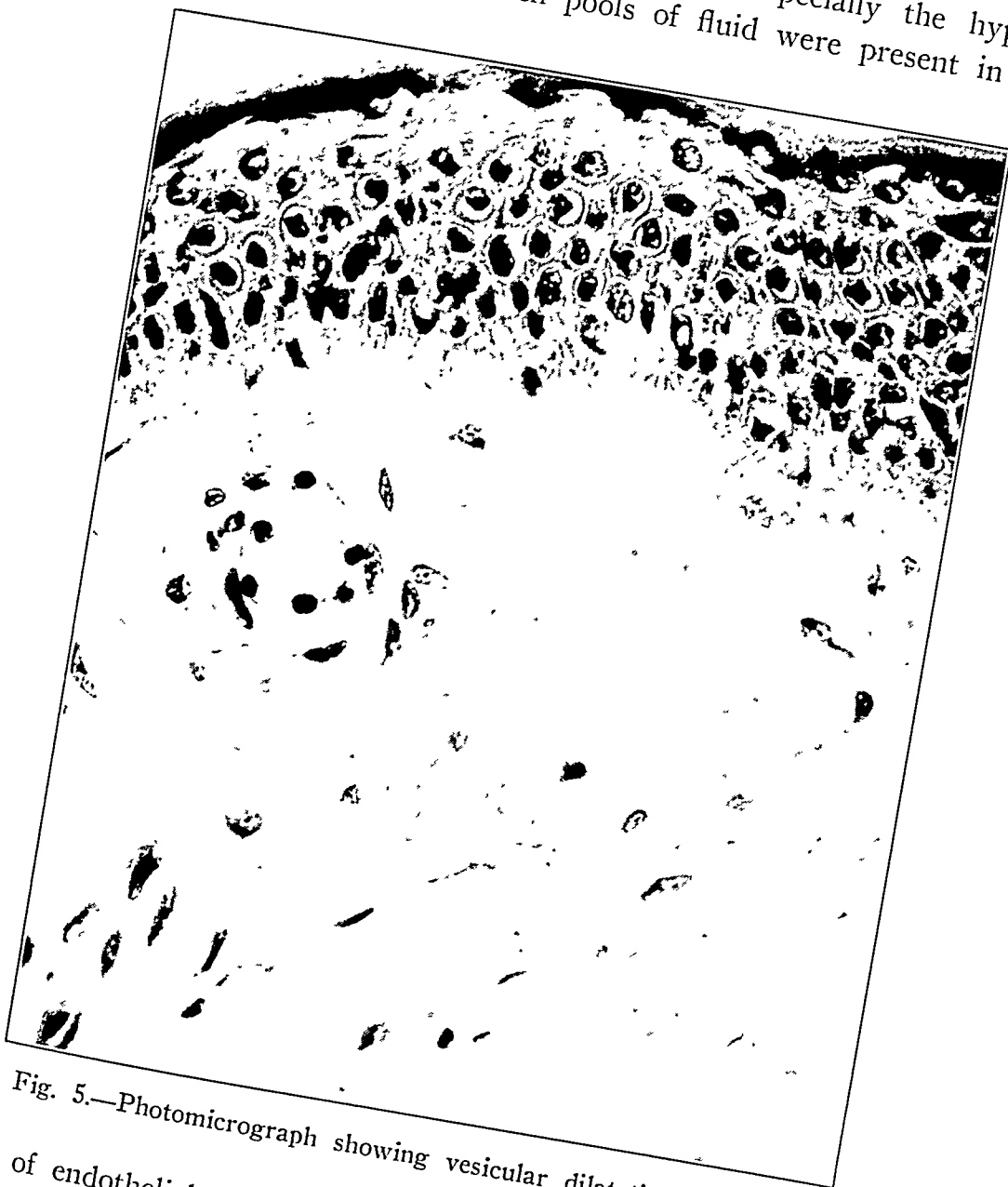


Fig. 5.—Photomicrograph showing vesicular dilatation ($\times 1,000$).

devoid of endothelial lining. They observed decided condensation of the papillary corium with some hyaline degeneration of the collagen, absence of the elastica and slight perivascular lymphocytic cellular infiltration.

24. McGuire, J., and Zeek, P.: Pathogenesis of Chronic Hereditary Edema of Extremities (Milroy's Disease), J. A. M. A. **98**:870 (March 12) 1932.

A biopsy specimen was taken from the calf of the right leg in the case reported, and the histologic sections were studied by T K Lawless, who gave the following detailed report

The stratum corneum is moderately hypertrophic, with no evidence of abnormal keratinization taking place. The granular layer is one cell in width through the entire section. The mucous layer is abnormally rich in cells characterized by vacuolar degeneration. The basal layer shows not only vacuolar degeneration but cellular separation due to increased edema. The basal line is almost straight. The principal changes in this condition take place in the corium. The papillary



Fig 6—Photomicrograph showing fibrosis and lymphatic dilatation ($\times 300$)

and subpapillary parts show a compression of the fibers with definite hypertrophy. The edema is pronounced, with many large, dilated channels without definite cellular walls. The elastic tissue, though showing signs of degeneration, is much in evidence. Blood vessels are present. They have thicker walls without perivascular infiltration. The reticular layer shows both hypertrophy and hyperplasia. The heavy collagenous fibers appear as short segments and show moderate degeneration. Edema is pronounced. The vessels are thickened, and the cellular reaction is slight. The subcutaneous tissue is characterized by the enormous open spaces, the paucity of normal cells and fatty infiltration. The appendages are all normal in appearance. The elastic tissue is fragmented and takes the stain poorly.

TREATMENT

A patient with an acute attack should be treated like one with an acute infection with local manifestations. When the deformity is great, the modified Kondoleon²⁵ operation is recommended. Properly fitted shoes gave my patient considerable relief. Rest and elevation of the legs at frequent intervals seem to be all that is needed in most cases.

SUMMARY AND CONCLUSIONS

Hereditary elephantiasis of the legs, generally known in this country as Milroy's disease, shows microscopically hypertrophy and increase of the connective tissue in the cutis, with edema and many dilated channels without cellular walls.

Two groups of cases can be recognized: (1) those in which the swelling is present at birth and (2) those in which the swelling appears in late childhood or in early adult life. The acute attacks are practically confined to the second group.

The case herein described belongs to the congenital group, and there were associated congenital anomalies which had not been previously noted, such as retention of the deciduous teeth, six toes on the left foot, congenital strabismus with amblyopia of the left eye and dystrophy of the hair.

25. Homans, J.: The Treatment of Elephantiasis of the Legs, *New England J. Med.* **215**:1099, 1936.

Clinical Notes

ULCERATIVE REACTION FROM GENTIAN VIOLET IN THE TREATMENT OF IMPETIGO CONTAGIOSA

LEON GOLDMAN, M D, CINCINNATI

Permanent scarring following uncomplicated impetigo contagiosa is rare. With the use of the occlusive method of treatment of impetigo with such agents as adhesive plaster or the less effective collodion, no deep extension of the lesion to an ecthymatiform ulcer has been observed. With the crusting type of therapy, no such ulcerations have been seen with silver nitrate, cupric sulfate or tannic acid-mercury preparations.

However, with the gentian violet crusting method this reaction has occurred occasionally in the past two years. It has been seen in 4 cases, in 2 infants and 2 adults. In these cases a smooth gentian violet crust formed over the impetigo areas. Instead of curling up, shrinking and peeling off, as the usual gentian violet crust does, the crusts in these instances remained fixed firmly to the skin for a relatively long period, more than two weeks and in 1 case five weeks. The skin adjacent to the adherent crust showed no redness, tenderness or edema. However, when the crust was removed, either with wet dressings or with scissors and forceps, a deeply punched-out area filled with pus was found. With irrigation and application of mercury ointments these areas healed rather rapidly but left ugly punched-out scars, some resembling a postvaricella scar and others the depressed scar of an ecthymatous ulcer. These were seen chiefly on the face and, in 1 infant, deep in the axilla. There was no evidence of hypersensitivity to gentian violet in any of the cases.

In 3 of the cases the solution of gentian violet used was a saturated alcoholic solution, containing approximately 30 per cent gentian violet. In 1 case, that of an adult, there were small depressed scars following impetigo spots treated with a 1 per cent aqueous solution of gentian violet. Other lesions on this patient's face, treated with 5 per cent ammoniated mercury ointment, showed no scars. The saturated alcoholic solution of gentian violet was used because of its excellent results in cases of impetigo of Bockhart and of pustular miliaria. Originally, it seemed to be desirable in impetigo contagiosa, in spite of the transient pain, because a firm heavy dry crust forms over the entire lesion in a few seconds to a few minutes, whereas the impetigo lesion treated with repeated applications of an aqueous solution of gentian violet continues to ooze for several hours. No bacteriologic studies were made of the material under the gentian violet crust.

In the gentian violet therapy of burns, when this form of therapy was more popular than it is today I would frequently observe failure of healing under the firm gentian violet crust but only rarely see persistent infection with deeper extension. I have had no experience with the gentian violet-silver nitrate treatment of burns.

This complication of the gentian violet treatment of impetigo contagiosa must be uncommon when one considers the popularity of this method. From the small group of cases here, the saturated alcoholic solution of gentian violet is much more apt to cause this. The complication should be suspected when there is no evidence of separation of a gentian violet crust after an arbitrary period of approximately

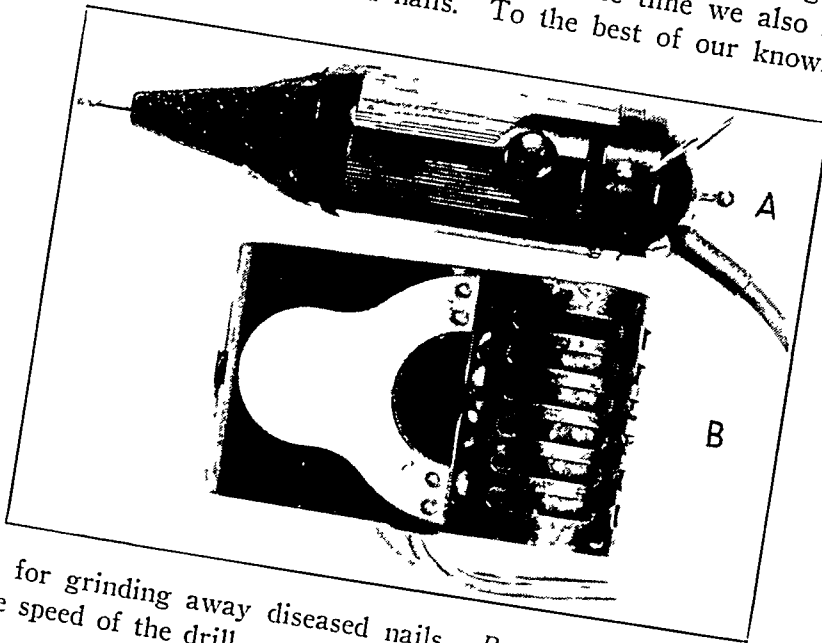
two weeks. This clinical survey does not suggest any reason why this reaction has occurred with gentian violet and not with the other occlusive or crusting methods. Perhaps if the other methods had been used as frequently as the gentian violet treatment, this unusual complication would have been encountered.

Carew Tower.

THE USE OF A DRILL ON DISEASED NAILS

ROY L. KILE, M.D., AND ASHTON L. WELSH, M.D., CINCINNATI

For many years chiropodists have used a drill for removing diseased nails and at times horny tissue from the feet. For some time we also have employed a drill for grinding away diseased nails. To the best of our knowledge, such an



A, a drill for grinding away diseased nails. *B*, a foot-controlled rheostat for regulating the speed of the drill.

instrument is not in general use by dermatologists. It is not expensive and may be equipped with a foot-controlled rheostat for regulating the speed. Steel or emery burrs of various shapes and sizes may be obtained to fit it. Two or three burrs will suffice for dermatologic purposes.

Diseased nails may be ground away much faster than they can be cut away and without causing any pain. Continuous running will cause the burrs to become warm and consequently cause some pain, but occasional short stops will prevent this. Much better application of drugs or physical therapy to the area is accomplished after the diseased nails are ground away with this or a similar instrument.

Abstracts from Current Literature

EDITED BY DR HERBERT RAITNER

MASSIVE DOSE ARSENOTHERAPY OF SYPHILIS BY THE INTRAVENOUS DRIP METHOD
H T HYMAN, L CHARGIN and W LEIFER, *Am J Syph, Gonorr & Ven Dis* 23 685 (Nov) 1939

Fifteen of the original series of 25 patients with early syphilis who were given massive dose arsenotherapy by the intravenous drip method are still under observation more than five years after treatment. The observations indicate that the massive therapy for five days without any other antisyphilitic treatment resulted in a complete cure in 13 of the 15 patients, or 86.6 per cent.

In the past two years a second series of 86 male patients with primary or secondary syphilis was treated. Four to 4.5 Gm of neoarsphenamine was administered during four or five days with the identical technic employed in the first series. Dark field examinations of material from moist early lesions showed negative results within twenty-four or forty-eight hours, and the lesions healed promptly. Seventy-eight of the second series are still under observation. Of the 78 patients, 67 (or 86 per cent) are entirely seronegative and are clinically well nine and fifteen months after treatment. The spinal fluids of 60 patients have been examined and are all normal. In 4 cases the treatment may be classified as a failure, and in 7 it gave doubtful results. In 6 of these 7 the result is doubtful because the Wassermann reactions have not as yet become entirely negative. In another man a new penile lesion of doubtful significance developed after he had exposed himself repeatedly to reinfection. Two patients have had a serologic relapse, and 2 others have had a clinical relapse (chancre redux).

Nitritoid crises did not occur in any of the treated patients. Febrile reactions occurred in the majority of the patients and were sometimes severe. A primary fever was present in more than 60 per cent, a secondary fever, usually associated with a toxicoderma, was observed in more than half the patients. Polyneuritis of moderate severity occurred in 10 per cent and was slight in another 25 per cent. There were no disturbances in renal function. One patient suddenly had a convulsion and died.

QUARTAN MALARIA IN THE TREATMENT OF NEUROSYPHILIS M M KROLL,
Am J Syph, Gonorr & Ven Dis 24 148 (March) 1940

The author reviews the literature and reports favorably on the use of quartan malaria in the therapy of neurosyphilis. In 5 out of 6 cases of primary atrophy of the optic nerve conservation of existing sight was achieved. No direct correlation was found between clinical and serologic improvement. There was 1 death as a result of quartan malaria in the 62 patients treated.

GRANULOMA INGUINALE L J ALEXANDER and A G SCHOCH, *Am J Syph, Gonorr & Ven Dis* 24 180 (March) 1940

A report of a case of granuloma inguinale is presented in which the pathognomonic giant cells of granuloma inguinale have been demonstrated in sections of tissue. The authors stated the opinion that the Giemsa stain is essential to demonstrate the typical giant cells in biopsy specimens, they were unable to demonstrate these cells with routine hematoxylin and eosin stains.

CHANGES IN THE LONG BONES OF NEWBORN INFANTS FOLLOWING THE ADMINISTRATION OF BISMUTH DURING PREGNANCY J WHITRIDGE JR, *Am J Syph, Gonorr & Ven Dis* 24 223 (March) 1940

The author confirms the previous work of Caffey, who described roentgenologic changes in the long bones of newborn infants whose mothers had received intra-

muscular injections of a bismuth compound during pregnancy as part of their antisyphilitic treatment. The roentgenologic changes consisted of transverse bands of increased density near the ends. The intramuscular administration of a bismuth compound to normal nonsyphilitic pregnant women produced similar changes in the long bones of the newborn infants, independent of the amount of the drug given. The changes are not due to healed syphilitic osteochondritis.

ON THE EFFECT PRODUCED ON NEWLY CONTRACTED SYPHILIS BY THE TRANSFUSION OF BLOOD TAKEN FROM PATIENTS AFFECTED WITH LATE STAGES OF SYPHILIS. M. S. BRAGIN, *Am. J. Syph., Gonorr. & Ven. Dis.* **24**:228 (March) 1940.

Repeated transfusions of blood from patients affected with late untreated syphilis to patients suffering from newly contracted syphilis produced a rather rapid reversal in the Wassermann reaction of the recipients' blood, which was, however, of only a temporary nature. There was no change in the Wassermann reaction of the patients' tissue fluid and but slight effect on the clinical symptoms.

Transfusion of normal blood did not produce any effect on the Wassermann reaction in patients with early syphilis.

REUTER, Milwaukee.

SYMPOSIUM ON ALLERGIC DERMATOSES: CONTACT-TYPE ECZEMATOUS DERMATITIS. MARION B. SULZBERGER, *J. Allergy* **11**:40 (Nov.) 1939.

In the author's opinion, the contact type of eczematous dermatitis is possibly the most common of all diseases of man, and in most instances, it can be proved to be allergic. Not all eczematous dermatoses are of allergic origin. The typical dermatosis produced by certain degrees of sunshine (*eczema solare*), the eczematous cutaneous lesions which are due to primary irritants, such as caustics, acids and alkalies, and the eczematous reactions from physical agents, such as heat, friction and maceration, are not allergic.

Allergens are usually not proteins or substances necessarily associated with proteins. Even simple chemicals, such as mercury, nickel and arsenic, are capable of sensitizing certain persons. Substances which can most easily penetrate through the natural protective layers of the skin, such as fat solvents, substances soluble in fats, keratolytics or detergents, are the commonest eczematogenous allergens.

The diagnosis of this form of dermatosis depends on the history, the clinical appearance and the course of the eruption, and *only in the last analysis on the results of the cutaneous test*. The results of patch tests are not conclusive; as in other cutaneous tests, they must be properly evaluated and correlated with other data.

The treatment is primarily *dermatologic*. The only approach from an allergic standpoint is the elimination of the causal agents. This is easy in some instances, difficult in others and in still others, unfortunately, impossible.

Desensitization is generally ineffectual, except possibly in cases in which the condition is due to plant oils.

The author finally points out that contact with the excitants need not necessarily be from without; it may be from within, providing the causal allergens reach the specifically sensitive shock tissue (epidermis?) in sufficient quantities (concentration) per unit of time and per size of area of skin. Cases of eczematous eruptions in which the condition appears after the injection or ingestion of quinine, methenamine, arsenicals or plant excitants are a few of many possible examples.

SYMPOSIUM ON ALLERGIC DERMATOSES: ALLERGIC DRUG ERUPTIONS. ADOLPH B. LOVEMAN, *J. Allergy* **11**:48 (Nov.) 1939.

A broad classification of drug eruptions would include all eruptions caused by drugs. The author limited the discussion to dermatitis medicamentosa—eruptions produced by the absorption and hematogenous spread of a drug or its split product. This absorption may result from ingestion, injection, inunction or even inhalation. Any drug, natural or synthetic, may produce a cutaneous or mucosal

hypersensitivity in some persons. There is considerable clinical and experimental evidence for judging dermatitis medicamentosa to be a manifestation of allergy.

The elicitation of the cutaneous response is not necessarily related to the amount of drug taken. Infinitesimal amounts of the drug may produce a cutaneous response, whereas, occasionally, tremendous doses of the drug may fail to produce an eruption in a person known to possess cutaneous hypersensitivity. Unquestionably, however, the extent, character and intensity of the eruption are related to the size of the dose.

Drug eruptions may appear days, months or even years after contact with the drug. On the other hand, an eruption may persist months, days or years after discontinuance of the use of the drug.

All drug eruptions, irrespective of their appearance, have characteristics in common. They appear suddenly, as a rule are bright red and have an atypically symmetric distribution, and the course is usually afebrile. Often they are accompanied by lesions on the mucous membrane, and, as a rule, the symptoms are mild.

The skin or mucous membrane are not the sole recipients of drug insults. Nerve pain, agranulocytosis, jaundice and headache have been observed after the ingestion of drugs. The author states the belief that many heretofore unknown visceral complaints may also be of drug origin.

SYMPOSIUM ON ALLERGIC DERMATOSES ALLERGIC REACTIONS TO PLANTS BEDFORD SHELMIER, *J Allergy* 11 56 (Nov) 1939

Flowers, vegetables and weeds produce more or less distinct clinical types of eruptions. Sensitization to flowers and shrubs has been observed by the author chiefly in housewives and occasionally in florists. The most frequent eruption has been of the recurrent, vesicular type, usually confined to the hands, forearms, face and neck. Flowers such as the shasta daisy, chrysanthemum, narcissus, iris and carnation have produced acute dermatitis of the severity of an ivy or primrose eruption.

Sensitization to vegetables and fruits has been of both the acute and the chronic type. It has occurred in housewives, grocery clerks and truck gardeners. The eruptions have been almost universally confined to the hands. The author observed contact dermatitis from spinach, tomatoes, radishes, mustard greens, corn, Irish potatoes, oranges, lemons, grapes and other fruits and vegetables.

Dermatitis from weeds usually involves all the exposed areas, face, neck, hands, forearms, ankles and legs. Vesiculation and swelling are only rarely encountered. Lichenification of the flexures is an outstanding characteristic of eczema due to weeds. The eruption is at first seasonally recurrent, but eventually it becomes perennial. Clinically these chronic conditions closely resemble generalized neurodermatitis. Those usually affected are farmers and farmwives, oil field workers, members of surveyor and construction gangs and others.

Weed-sensitive persons present a polyvalent sensitivity, they should be tested with all the common weeds in their environment. The fresh leaf, portions of the dried plant and the extracted oleoresin may be used for patch tests.

Oleoresins are the best testing material. The author describes his method of preparing oleoresins, which is extracting with ether and acetone.

Best results of treatment have been in persons who have avoided further contact with weeds. Hyposensitization by intramuscular injection or ingestion of the antigenic oils gave poor results. Some patients, however, felt that they have either been desensitized or greatly benefited by the oral administration of the antigenic oleoresins.

SYMPOSIUM ON ALLERGIC DERMATOSES INFANTILE ECZEMA RUDOLPH HECHT, *J Allergy* 11 195 (Jan) 1940

Infantile eczema is not a well defined condition. Hill has subclassified the group into seborrheic dermatitis, contact dermatitis, eczematous fungous eruptions and atopic dermatitis. Any one or more of these may be present in the same

person, and one form may be transformed into another. The differentiation of the various types from one another is sometimes impossible.

The diagnosis of infantile atopic dermatitis is based on a family history of atopy, the presence of immediate wheal type reactions to scratch or intracutaneous tests with the usual atopens, negative results to patch tests with contact substances, the presence of reagins in the serum and eosinophilia. Morphologically, there is an erythematous, papulourticarial, vesicular, frequently weeping eruption usually occurring on the face and neck and accompanied by violent uncontrollable itching.

Environmental substances, such as house dust and feathers, play a significant role in infantile eczema. The removal of these substances plus elimination of certain foods offer better results than just the elimination of certain foods. The best method of treatment is careful dermatologic management, including proper choice, application and removal of local remedies, bandaging, careful splinting to prevent scratching, avoidance of soap, the use of sedatives and general hygienic and medical care.

SYMPOSIUM ON ALLERGIC DERMATOSES: ATOPIC DERMATITIS. BEN Z. RAPPAPORT, J. Allergy **11**:200 (Jan.) 1940.

The morphologic characteristics of the childhood and adult types of atopic dermatitis differ from those of the infantile type. The former types merge, one into the other, morphologically. The lesions are no longer vesicular and develop in definite areas of predilection: the forehead, scalp, sides of the neck, the wrists and the flexures of the elbows and knees.

In a large proportion of cases the condition clears with or without treatment at the age of 2 years, with no recurrences. In others, there is a recurrence at about the age of 5 to 7 years. After months or years the condition clears up in some, either permanently or with recurrences at puberty. If there are recurrences at puberty the condition lasts until the patients are in their twenties or thirties, when, with or without treatment, it clears in most patients.

There is a definite seasonal occurrence or flare-up in many cases. A large group of patients are worse in the winter, and in others the symptoms develop at the beginning or at the height of the various pollen seasons. The majority of patients in the latter group have concomitant symptoms of hay fever.

Some of the cases occurring during the summer have shown definite improvement after pollen hyposensitization. The results of such treatment, however, have not been uniform in the hands of the author.

Foods as a cause of atopic dermatitis are more important in the child than in the adult. The importance of the immediate wheal type of reaction with various atopens is controversial. The author found them of greater value in children than in adults. The most practical approach for adults is to place the patient in a carefully controlled environment, with unusual care in the way of dust-free precautions, and then to treat the condition by topical means. Elimination diet studies are of importance, primarily in childhood.

It is strange to see a patient improve rapidly in a hospital room and then, with practically identical furniture and food at home, suffer a relapse, only to improve again on hospitalization. There may be many atopens in the home that have not been recognized as causes of trouble.

SYMPOSIUM ON ALLERGIC DERMATOSES: FUNGUS ALLERGY. SAMUEL M. PECK, J. Allergy **11**:309 (March) 1940.

The same organism, whether a bacterium or a fungus, can give rise to totally different syndromes, while unrelated pathogens can initiate practically identical pictures. Eruptions due to micro-organisms can be divided into two classic types: (1) typical forms, which are due to fungi themselves, and (2) atypical forms, referred to as cutaneous microbids. The latter depend for their develop-

the interaction between bacteria and fungi, or their products, and the allergic skin. Tuberculids, trichophytids and levurids are classic examples of cutaneous microbids.

The epidermophyton and trichophyton fungi grow in the nonliving layers of the skin and its appendages. Inflammatory reactions do not develop until the living structures are involved, when hypersensitivity with its resulting allergic manifestation is brought about. This sensitivity is revealed by a positive trichophytin reaction which is specific for the group in the majority of instances. The period between onset of infection and development of hypersensitivity varies from a few months to several years.

Continuous maceration, trauma, application of strong ointments or even x-ray rays force the fungi or their products into the blood stream. These in turn, coming in contact with the hypersensitive skin, give rise to trichophytids.

The diagnosis of microbids is made with great frequency and often without proper supporting evidence. The author lists criteria for the establishment of such a diagnosis. An instructive classification of trichophytids is included.

The reaction to the trichophytin test is not always the same in degree throughout the year. The author found that the reactions were more strongly positive during periods of exacerbation of the primary focus. False positive reactions are often due to secondary bacterial contamination or to the ingredients of the mediums themselves.

The immediate reaction to trichophytin is rare, patients manifesting such reactions usually do not have the delayed type of reaction.

The reaction after injections of oidiomycin is positive in practically 100 per cent of adults, but in infants and young children positive reactions are rare.

The results of use of trichophytin as a therapeutic measure were disappointing. Recently, however, the author observed improvement of patients with trichophytids by the injection of trichophytin.

SYMPOSIUM ON ALLERGIC DERMATOSES ALLERGIC OCCUPATIONAL DERMATOSES **LOUIS SCHWARTZ, J. Allergy 11:318 (March) 1940**

Many cases of occupational dermatoses seemingly due to allergy can be explained by changes in working conditions, by variations from the normal in the skin of the worker or by breaks in the defense mechanism of his skin. In a compilation of about 10,000 cases of occupational dermatoses made from the reports of various state compensation boards, allergy was the cause of the dermatoses in less than 18 per cent of the cases.

In allergic occupational dermatitis, the period of incubation is usually eight to twenty-one days, although it may be longer. A dermatitis which develops in less than a week after exposure to an irritant is usually not due to allergy acquired from that particular job. On the other hand, a worker may get an allergic occupational dermatitis even three weeks after leaving a job in which he was exposed to sensitizers.

The patch test gives a rapid, although not altogether reliable, clue as to the allergic origin of an occupational dermatitis. If the dermatitis was or is generalized and the reaction to patch tests with great dilutions of chemical spreads, if the dermatitis—if still present—becomes exacerbated as a result of the patch test, if areas of healed dermatitis light up anew or if new areas of dermatitis develop and constitutional symptoms follow the application of the patch test, then allergy is probably present.

The author includes a list of chemicals which he found to produce allergic occupational dermatitis. Some chemicals, such as the chromates, many essential oils and insecticides, are primary irritants in strong concentrations and sensitizers as well. Allergy to finished dyes, so often seen among the wearers of dyed clothing, is not common among the workers engaged in manufacture of dyes.

Spontaneous desensitization may occur in industry. Occupational exposure first causes a sensitivity, and then, after the exposure continues, an immunity develops.

in some cases—the workers become “hardened.” Workers in whom such an immunity does not develop should be transferred to other occupations. Attempts to desensitize by giving minute increasing doses of the sensitizing agent have met with success in only a few isolated cases.

MENDELSON, New York.

DERMATOLOGY AND FOLK-LORE. J. D. ROLLESTON, Brit. J. Dermat. **52**:43 (Feb.) 1940.

Aside from being of interest, this article is an excellent source of material for those interested in medical folklore.

PSORIASIFORM CARCINOMA OF THE PENIS. LOUIS SAVATARD, Brit. J. Dermat. **52**:87 (March) 1940.

Savatard includes under the title psoriasiform carcinoma lesions of erythroplasia of Queyrat, Paget's carcinoma and Bowen's disease. There is some variation in the clinical appearance of these lesions, just as there may be in psoriasis; the color may be bright red, pink, dull red, brownish red or even brown. The diagnosis is made by histologic examination. The term “psoriasiform” is merely descriptive of the clinical picture, in the same sense that the term “morphea-like” is used in “morphea-like epithelioma.”

ENVIRONMENT AND SKIN DISEASE. F. F. HELLIER, Brit. J. Dermat. **52**:107 (April) 1940.

This paper presents an analysis of figures based on patients attending the dermatologic department of the General Infirmary at Leeds, with particular attention given to the effect of climatic changes on the incidence of various cutaneous diseases. The patients were from an industrial town of half a million inhabitants, employed in many different trades, including the manufacture of iron and steel, coal mining, printing and all the processes associated with the manufacture of cloth.

The incidence of eczematous eruptions, including both exogenous dermatitis and constitutional dermatitis, when studied with respect to monthly incidence in the community was found to be remarkably constant, but there was a high incidence of industrial dermatitis.

Infantile dermatitis, on the other hand, showed peaks in the spring and autumn, and in an effort to explain these peaks the figures were studied with respect to barometric pressure, wind, cold and other factors, because infants are least exposed to the influence of external irritants. There was not an accurate correspondence between the months with the lowest barometer readings and those with the highest incidence of eczema, nor was severity of cold an important factor in the variations from year to year in the incidence of infantile eczema. No relation could be found between eczema and the relative humidity, though, if anything, the wetter springs were associated with a somewhat greater incidence of eczema; there was a slight decrease of incidence with a higher drier temperature.

Hellier concludes, however, that these factors, although not fundamental factors in infantile eczema, may play a small part in that during the spring months they are all acting in the same direction. In the spring there is an increase of irritability of the skin completely independent of any direct action of external factors. This increased reactivity occurs with other changes in the spring, such as increased sexual activity, and these are part of the rhythm found throughout the whole animal kingdom.

Urticaria had its great frequency in autumn, but there were not enough data to permit the drawing of any conclusions. Psoriasis seemed definitely to be influenced by the number of hours of sunshine, and the figures indicated that the influence of the sunshine on the skin operates for a considerable time after

exposure Rosacea showed a definite association with cold weather Other diseases, such as scabies, lichen planus, carcinoma and impetigo, were investigated with respect to their relative incidence and were not studied from the viewpoint of the effect of environment on them

RATTNER, Chicago

THE LOCAL TREATMENT OF ULCERATED ORIENTAL SORE BY THE POWDER OF CERTAIN SULPHONAMIDE DERIVATIVES F AKRAWI, J Trop Med & Hyg 43 4 (Jan) 1940

Baghdad, Iraq, is the largest endemic center for oriental sore in the world The ulcerated phase of the disease offers a difficult therapeutic problem Local treatment by paints and ointments is unsatisfactory in most cases Physical agents, such as cauterization, coagulation and application of solid carbon dioxide, frequently give rise to keloids Solid carbon dioxide, however, is the best of the three aforementioned treatments Roentgen ray therapy is to be recommended The authors state that the internal administration of an antimony preparation produces but a small percentage of cures The author treated the ulcerated forms of the disease by means of sulfanilamide and sulfapyridine powder After the lesion was cleansed with saline solution, the powder was applied daily until complete healing was obtained If the period of treatment exceeded one month the treatment was discontinued, and the case was registered as unsuccessful Absolute cure took place in less than one month in 63 per cent of the author's cases, an unusually short time for ulcerated Baghdad boils

LAYMON, Minneapolis

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

HERBERT RATTNER, M.D., *President*

M. H. EBERT, M.D., *Secretary*

April 17, 1940

Keratosis Follicularis (Darier). Presented by DR. N. C. BARWASSER (by invitation) and DR. E. B. RITCHIE (by invitation), Davenport, Iowa..

W. L., a married white man aged 37, states that the eruption first began when he was 5 years old, on the hands and neck. When he was 21, the condition had become generalized. On three occasions he has had acute flare-ups involving the face and the scalp, with swelling of the glands of the neck.

He has had pneumonia twice within the past twelve years, and during these attacks the cutaneous condition improved. A corneal opacity of the right eye developed ten years ago following an injury.

The family history reveals a strain of mental instability, selecting the male side of the family. One older brother has Parkinson's disease. The mother and three sisters are living and well.

The eruption consists of brownish follicular keratotic papules, which average 4 mm. in diameter, of almost universal distribution, more confluent toward the middle portions of the body. There is a background of dusky erythema particularly noticeable on the face. The legs are encased in a mass of heaped-up dry, tightly adherent scales. On the palms and soles there are well defined areas of keratosis. On the mucous membrane of the hard palate there is a diffuse whitish verrucous patch.

Laboratory examinations revealed nothing of significance except a leukocyte count of 8,300 per cubic millimeter, with 8 per cent eosinophils. The biopsy specimen showed the histologic picture of Darier's disease.

Treatment has consisted of about forty-five intravenous injections of gold and sodium thiosulfate, with an average of 30 mg. per dose. Both grenz rays and roentgen rays have been used on selected areas on the legs.

A Case for Diagnosis (Keratosis Follicularis [Darier]?). Presented by DR. THEODORE CORNBLEET.

J. D., a white man aged 21, presents an eruption on the back, shoulders and neck of two years' duration. The condition is not very pruritic. The lesions consist of light red papules, varying in size from that of a pin to that of a match head. They have a tendency toward follicular involvement and some are verrucous.

DISCUSSION

DR. C. W. FINNERUD: Both patients show unusual examples of Darier's disease. One has probably the most extensive condition that has ever been seen. Dr. Cornbleet's case should be studied histologically to make the diagnosis certain.

DR. E. B. RITCHIE (by invitation), Davenport, Iowa: An interesting feature in the family history of the first patient is that his younger brother has Parkinson's disease, indicating a possible familial ectodermal defect.

DR. DAVID LIEBERTHAL: The subsequent history of a patient I reported on in 1904 (Lieberthal, D.: A Case of Darier's Disease, *J. A. M. A.* 43:242 [July 23] 1904) disclosed that several cases of a similar condition of the skin occurred in three generations of his family.

A Case for Diagnosis (Congenital Dyskeratosis and Leukokeratosis Oris?). Presented by DR N C BARWASSER (by invitation) and DR E B RITCHIE (by invitation), Davenport, Iowa

E Y, an unmarried white man aged 23, born of Slavic parents, is by occupation a miner. There is nothing of significance in his medical history or in the family history. He graduated from high school at the age of 19.

He had warty lesions about the eyes and lips at birth. When he was 3 years old the lower lip became so pendulous that it required a surgical operation. Hoarseness has been present since early childhood. Two years after a tonsillectomy, when he was 11 years old, changes were first noticed in the mouth. When he was 12 years old warty lesions appeared on the backs of the hands. Since then the legs, arms, feet, lumbar vertebral region and gluteal folds have become involved. Bullae are said to have occurred through this progression, although not definitely related to trauma.

The patient presents a dry vegetative flesh-colored dermatosis involving the upper and lower eyelids, producing a well defined rim measuring 4 mm in width and 2 mm in elevation. There is some thickening about the nares. The lips are thickened and show the same type of vegetative process, which blends gradually with the skin of the circumoral region. In the glabellar region there is a less well defined area of smooth hypertrophic change. A small soft flesh-colored nodule is present on the helix of each ear. The mucous membranes of the mouth are thickened, whitish and coarsely verrucous. The tongue is small and hard and limited in movement. There are leukokeratotic changes over the entire tongue. The teeth are in advanced stages of caries, widely spaced and peg shaped. On the extensor surfaces of the elbows, forearms and knees, the tibial aspects of the legs, the dorsa of the feet, the lumbar vertebral region and the gluteal folds, extending down to and surrounding the anus, are variously sized, discrete and confluent, dry hypertrophic plaques, showing scaling and slight erythema. Within these areas are many acutely inflamed lesions with necrotic centers. There are also faint cribriform atrophic lesions of various sizes both within these hypertrophic areas and elsewhere, noticeably on the flexor surfaces of the forearms. On the dorsa of the feet and hands, as well as on the palms and soles, there are discrete areas of dry, brownish, sharply pointed, verrucous lesions.

The nails of the fingers and toes are normal. The body hair shows no abnormality. There is no hyperhidrosis.

The Kahn test gave a negative reaction. The red blood cell count was 4,600,000 per cubic millimeter, with 90 per cent hemoglobin, and the white blood cell count was 6,800 per cubic millimeter, with a normal differential count.

The biopsy specimen taken from the back of the hand showed the epithelial surface to be thrown into sharp pointed folds. There was intense hyperkeratosis, thickening of the stratum granulosum and acanthosis, with some intercellular edema. There was round cell infiltration scattered throughout the upper portion of the corium. The blood vessels showed some dilatation.

DISCUSSION

DR RUBEN NOMLAND, Iowa City. I saw this man several months ago. After looking up the literature I thought that he presented a syndrome of ectodermal defect, as in cases of pachyonychia congenita recently described. He has much less involvement of the nails than in most cases of this disorder, but it is like a good many that have been described. It is also like the case that Dr Cole (*ARCH DERMAT & SYPH* 21 71 [Jan] 1930) described, in which he differentiated between these ectodermal defects.

DR M H EBERT. In looking at the mouth of this patient with Dr Wile, we both noticed the resemblance between the lesions in the mouth and on the tongue and the lesions in a case of amyloidosis that was presented at the meeting in Ann Arbor. The rest of the syndrome showed no resemblance. It is possible that in these lesions amyloid might be demonstrated.

SOCIETY TRANSACTIONS

DR. N. C. BARWASSER (by invitation): I am indebted to Dr. Nomland for some fine pictures and also for his opinion on this case. One feature that impressed me is that there were no apparent changes in the nails.

Atrophia Pilorum. Presented by DR. E. E. STENHOUSE (by invitation).

Miss M. E., a stenographer aged 24, states that the hair of the scalp was normal until she was 14 years of age. At that time she noticed two areas on the vertex in which the hair became thin and short. At no time were the areas bald. Hair gradually grew in these areas again, but it was short and thinner than before.

When she was first seen in September 1938, there were several small areas in which the hair was short (from 1 to 2 inches [2.5 to 5 cm.]), coarse and dry. These areas gradually enlarged, until now there is short fine hair over the entire scalp except about the ears and at the nape of the neck. The hair in the involved areas now seems to be of more normal texture but finer and thinner. At no time has there been inflammation or evidence of disease of the hair, bulb or shaft. There is no splitting at the end of the hair. The hair on the other parts of the body is normal.

About two months ago the finger nails became pitted to such an extent that the pits appeared to be in transverse ridges.

Her general health is good. Her only complaint is fatigue after a day's work. The serologic examination of the blood gave negative results; the urine was normal. There is a mild grade of secondary anemia. The basal metabolic rate last week was —24 per cent.

Treatment has included local treatment of the scalp, administration of thyroid, of vitamins and of hematinics and ultraviolet irradiation.

Atrophia Pilorum. Presented by DR. S. W. BECKER and DR. M. E. OBERMAYER.

Miss E. J. was first seen in July 1935, at the age of 19, complaining of partial loss of hair of four years' duration. The alterations took place in about two months, during which time the hair over the vertex tended to fall out more freely than normally, and new hair in that region was short, about 2 cm. in length. The hair at the inferior portions of the scalp and in the nuchal region retained its normal length.

Various methods of therapy have been used, with no improvement. Physical examination showed no abnormalities. The Kolmer and Kahn reactions of the blood serum were negative. There is no history of a similar condition in the family.

Microscopic examination of the hair showed it to be atrophic, but there were none of the signs characteristic for monilethrix or trichorrhexis.

DISCUSSION

DR. S. W. BECKER: When we first saw this patient some years ago I tried unsuccessfully to find a similar condition in the literature. It is striking that this young girl retains normal hair at the fringe, as do some bald men. The condition is not premature alopecia, because the hair is present over the vertex, but it is atrophic and persists in its atrophic state.

Pyoderma Faciale. Presented by DR. HERBERT RATTNER and DR. THEODORE CORNBLEET.

Miss E. H., a white American aged 30, states that she had no trouble with her skin until six or seven years ago, when occasionally pimples appeared on her face. There were not enough for her to seek medical attention until about a year ago, when the condition became suddenly worse. With ointments and ultraviolet ray therapy during the summer and fall of 1939 the condition improved. In January 1940 there was an exacerbation, for which she again received treatment with ultra-

violet rays and a liquid medicine, which, according to her physician, contained ferrous sulfate, diluted sulfuric acid, potassium sulfate, magnesium sulfate and water. New lesions continued to develop, and for the past two months she has been forced to give up her employment. She has not taken any iodides or bromides. Her menstrual periods have been regular, every twenty-eight days, without dysmenorrhea. Aside from a nervous breakdown and gastrointestinal complaints when she was 20, she has always been in good health.

The physical examination showed no abnormalities. A number of teeth have silver fillings. The skin of the forehead, cheeks, nose and chin shows cyanotic erythema with some puffiness. The skin around the eyes is normal. The involved portions are composed of superficial and deep abscesses and cystic lesions which seem to communicate with one another. The surface is studded with pustules of various sizes, especially around the mouth and chin, and dried honey-colored crusts are scattered about the surface of the lesions. Pitted scars are visible on the cheeks. Isolated pustules and cystic lesions are scattered on the neck and the central area of the chest. No comedos are seen.

Laboratory Tests—The urine was normal. Examination of the blood showed 78 per cent hemoglobin and 4,150,000 erythrocytes and 13,650 leukocytes, per cubic millimeter, with 77 per cent polymorphonuclear leukocytes, 2 per cent eosinophils, 16 per cent lymphocytes and 5 per cent monocytes. The basal metabolic rate was —5 per cent. A roentgenogram of the chest showed no pulmonary changes. A Mantoux test, with a dilution of 1:10,000 of old tuberculin gave a positive result. The Kahn test gave a negative reaction.

DISCUSSION

DR PAUL A. O'LEARY, Rochester, Minn. This condition is typical of the eruptions Dr Kierland and I recently described as pyoderma faciale (*ARCH DERMAT & SYPH* 41:451-462 [March] 1940). The disease is characterized by an explosive eruption on the face of women in their early twenties who have not had preceding acne. The characteristic lesion is the deep pustule, with subsequent development of tunneling abscesses and resulting keloid. Comedos, not only on the face but also on the chest, are conspicuous by their absence. These patients are underweight and anemic and frequently have amenorrhea. Efforts to attribute the eruption to a focus of latent tuberculosis elsewhere in the body have failed. Histologic section, tuberculin tests and guinea pig inoculations have not thrown any light on the problem. The point that Dr Kierland and I endeavored to stress is that the therapeutic program should be mainly directed to the patient's systemic status, giving treatment for the anemia or amenorrhea and prescribing rest in bed and high vitamin diet. The local measures of draining the abscesses, roentgen ray irradiation for the keloidal scarring and application of a mild sulfur preparation should be carried out simultaneously. The explosive onset of the eruption in a person who has not had acne vulgaris and who manifests few comedos characterizes the disease.

DR FRANCIS E. SENEAR. Dr O'Leary not only has given a good description but has given the condition a name. The condition in these cases does not fit any other particular description of acne. I for one am glad to have a name for cases of this type.

I should like to ask Dr O'Leary if this condition occurs in persons of the rosacea age. Most of the examples I have encountered have occurred in a much younger age group.

DR S. W. BECKER. I have had a few cases. The facts that the condition occurs in patients of the rosacea age and resembles rosacea led me to think that it was simply a severe form of rosacea. Treatment has been the same as Dr O'Leary's, sunshine and rest, which results in great improvement.

DR H. E. MICHELSON, Minneapolis. I still feel that this condition belongs to the acne group. I have seen it, of course, many times and I believe that when the pustules are opened comedos can be found in the pus. Although some patients do not respond to the treatment employed for acne, many do.

DR. HERBERT RATTNER: I can recall having encountered several such eruptions that belong, I think, in the group of pyoderma faciale. I did not know where to classify them, for the condition differed from ordinary severe acne, and certainly it was not an example of rosacea.

Generalized Scleroderma. Presented by DR. HERBERT RATTNER and DR. THEODORE CORNBLEET.

Mrs. B. T., a Negress aged 39, was well until about two years ago, when she started to vomit an hour or so after meals. There was no pain. At the same time she noticed an increased pigmentation of the skin, especially of the neck and face, which gradually involved the entire surface of the body. In time the pigmentation became lighter, so that the skin became depigmented and mottled, first on the neck, face and chest and later on the extremities. About eighteen months ago, her hands commenced to swell, the condition lasting a few weeks, after which the skin remained tense and shiny with restricted motion of the fingers. Recently she has noticed decreased ability of the jaws to move and inability to protrude the tongue beyond the lips. There has been a gradual loss of hair from the scalp. Her appetite has remained good, but she has lost 40 pounds (18 Kg.) in the last two years, with a loss of strength. She also complained of coldness and numbness of the extremities.

The patient has had four pregnancies. The first occurred when she was 16, and she bore a full term normal child, who is now 24 years of age. The next three pregnancies resulted in spontaneous miscarriages at four months, with considerable loss of blood each time. Her menstrual periods have occurred regularly every twenty-eight days, even through the present condition.

Her father and mother are living and well, aged 80 and 73 years, respectively, as are two sisters and four brothers. There is no similar disease in the family.

Physical examination reveals a somewhat emaciated Negress with sparse hair on the scalp and a masklike expression on the face. The neck has a mottled appearance, with light linear streaks running perpendicularly on the anterior surface. All the skin of the body is hidebound, rigid, shrunken and atrophic, with a glossy sheen, especially over the extremities. Pigment is retained about the follicles, giving a dotted appearance to the skin.

Laboratory Tests.—The urine was normal. The Kahn reaction was negative. The basal metabolic rate was —3 per cent. The cholesterol content of the blood amounted to 219 mg., the calcium to 8.46 mg. and the phosphorus to 4 mg. per hundred cubic centimeters. The nonprotein nitrogen, creatinine and sugar contents of the blood were within normal limits. Roentgenograms of the chest, the bones of the right hand and the gastrointestinal tract were normal. The histologic picture was compatible with the diagnosis of scleroderma.

DISCUSSION

DR. S. W. BECKER: This patient presents an interesting course of events from the standpoint of pigmentary disturbance. In the first place she was a rather light-skinned Negress. Then she became dark over most of the body; later she became depigmented, and at present she is regaining pigment, first of all between the follicular orifices. Dr. Oliver called my attention to the fact that Negroes become depigmented with the use of rubber gloves. This loss of pigment between the follicles, with pigment returning first of all in the follicles, suggests that in some of these conditions the follicular pigment is the last to be lost.

DR. E. A. OLIVER: An interesting feature in these cases of depigmentation is the behavior of the pigment in the hair follicles. It is the last to disappear and the first to reappear. Another peculiar thing in the group of cases of leukoderma was that the hairs remained unaffected; none of them were depigmented. More will be learned about pigment formation as unusual cases are encountered.

In examining sections, Dr Weidman found that the cells of the granular layer of the epidermis gave dopa reactions and that there were dopa-positive granules in the stratum corneum and in the secretory cells of the sweat glands

DR HERBERT RATTNER This patient has shown considerable improvement both in general well-being and in the cutaneous lesions from treatment with histamine induced by iontophoresis

NOTE—The patient subsequently died of pneumonia

A Case for Diagnosis (Infectious Dermatitis?) Presented by DR M H EBERT

M B, a white woman aged 50, presents an eruption on the dorsum of the left forearm and left wrist and on the right leg near the knee About seven months ago the first lesions appeared as moderately itchy papules on the dorsum of the left hand About four months ago similar lesions appeared on the areas involved at present The lesions spread peripherally and cleared centrally

The lesions are gyrate and appear to have been formed by the coalescence of coin-sized annular lesions A threadlike, raised margin, 1 to 2 mm across, is made up of vesicopapules which have coalesced The central area is slightly hyperpigmented but not atrophied

Histologic examination showed the following picture Most of the stratum corneum had been exfoliated The remaining lamellas were parakeratotic The stratum granulosum was absent The rete mucosae was acanthotic There was intercellular and intracellular edema In places there was decided migration of the leukocytes through the rete, with the formation of microabscesses in the upper part of the rete The upper part of the corium was edematous A slight perivascular round cell infiltrate was present

DISCUSSION

DR C W FINNERUD I do not know what the eruption is, but I believe it probably fits in better with erythema annulare centrifugum than with anything else, after considering the clinical and histologic observations I feel rather strongly that the condition is not psoriasis or lichen planus

DR M R CARO I thought that histologically most of the conditions mentioned could be ruled out except psoriasis There were certain changes, like microabscesses and changes in the papillae, that would suggest psoriasis

DR M H EBERT This case has been rather confusing When I first saw the patient the lesions were dry, with little scaling and with a threadlike border I concluded that clinically the disease was erythema annulare centrifugum On looking at the sections I was struck by the presence of microabscesses and also of microscopic vesicle formation, as well as by the great amount of acanthosis, more than one would expect in psoriasis The next time I saw the patient, which was two days ago, the clinical appearance bore out the impression gained from the histologic section in that there were tiny vesicles present in this border Two days later they began to disappear In two or three weeks little spread has occurred, so the condition could not be called erythema annulare centrifugum unless it is just starting I did think of infectious dermatitis with a centrifugal spread Examinations were made for fungi, but none were found

Psoriasis with Pustular Exacerbation Presented by DR DAVID V OMENS and DR WALTER W TOBIN (by invitation)

K B, a woman aged 52, states that six months ago a red, itchy eruption appeared on her thighs, beneath the breasts, about her ears and on the feet, hands and arms It became progressively more severe, necessitating hospitalization Within the past three weeks, and since she left the hospital, the eruption has become worse

The past history is essentially not significant

Examination discloses diffuse erythematous, crusted dermatitis on the upper, inner parts of the thighs, in the groins, beneath the breasts, about the face and ears and on the forearms. There are numerous small discrete abscesses in the aforementioned areas and especially on the dorsa of the hands, toes, forearms and knees and about her ears.

The blood and urine were normal. Biopsy of a pustular lesion showed typical psoriatic changes with a large epidermal pustule and a lymphocytic infiltrate in the corium below it.

DISCUSSION

DR. HARRY R. FOERSTER, Milwaukee: I believe that the condition may be moniliasis in a patient with psoriasis, because of the type of lesion in the non-intertriginous areas. The changes in the nails are suggestive of psoriasis, and the lesions under the breasts, while suggesting moniliasis, have features that psoriasis may exhibit in such localities. The lesions in flexural areas are more infiltrated than typical monilial eruptions. The fissured lesions at the corners of the mouth are the only ones that cannot be explained in a diagnosis of psoriasis.

DR. DAVID V. OMENS: This patient was in the hospital three or four months ago, and at that time she presented a similar picture, but the condition was not as pustular as it is now. At that time the resident made a microscopic examination and found *Monilia*. She was treated with dressings soaked in potassium permanganate solution and seemed to do well. I saw her two days ago for the second time, and she had an acute exacerbation. The first time she presented diffuse pustules in these patches. She shows considerable change in so short a time, e. g., two days.

DR. OLIVER S. ORMSBY: Some years ago Ebert (Ebert, M. H.: A Psoriasiform Eruption with Pustular Exacerbation, *ARCH. DERMAT. & SYPH.* **27**:933 [June] 1933) reported on 2 patients (sisters) who had been under my observation for a number of years. The first patient had had recurrent attacks of some cutaneous condition since infancy. When she was 12 years old psoriasiform lesions developed on the elbows, trunk and scalp. Later the lesions on the scalp became pustular, and a general exfoliative dermatitis supervened, lasting a year and a half. During my observation of this case, which included several periods in the hospital, the disease ran a varied course. When it was comparatively quiescent, plaques of ordinary psoriasis were present on the extensor surface of the arms and on the back and legs, and there were scaling lesions on the scalp. During an active attack the plaques became acutely inflamed and were surrounded by an areola, with the development of numerous pustules. The plaques increased in number and were found in the usual areas of psoriasis. The inflammatory areola was often beset with numerous minute intradermic pustules, and the lesions felt hot and were tender. All the nails were involved. During an acute attack the temperature became elevated, and there was leukocytosis (15,000 leukocytes per cubic millimeter).

In the height of an attack the eruption became extensive and presented numerous flat pustules generally distributed, together with much cutaneous edema. After ten days the acute phase subsided, leaving only psoriasiform plaques.

An exactly similar condition existed in the patient's sister, which consisted of recurring attacks, which at times developed into general exfoliative dermatitis with psoriasiform plaques in the quiescent stage and pustular lesions together with lesions of infectious dermatitis in the more active phases.

Pustular psoriasis of Barber, which is largely limited to the hands and feet, is different from the condition in the cases described and in the case shown today. Dermatitis seborrhoeica and a mycotic (yeast) infection should be considered in this case. A period of observation may show definitely that the condition is psoriasis with pustular exacerbation.

DR. DAVID V. OMENS: We have not given her sulfathiazole. We have given her sulfanilamide but not enough as yet to obtain results.

A Case for Diagnosis (Gangrene? Toxic Eruption?) Presented by DR HERBERT RATTNER and DR IRENE NEUHAUSER (by invitation)

R B, a white woman aged 41, was admitted to the hospital two weeks ago. She states that immediately prior to her illness she had been well and that one week before admission she noticed that her nose was beginning to swell, the swelling gradually spreading over the upper portion of her face, causing her eyes to close. Also severe intermittent pain developed in her left leg, and there were redness and swelling of the lower third of the right leg.

In 1929 the patient was in Cook County Hospital with an illness which was apparently similar to the present one, swelling of the face and tongue, which resulted in gangrene and sloughing of the left ala nasi. Also necrosis developed in some of the small nodules which appeared on the lower extremities. At that time a diagnosis of erythema multiforme was made.

On admission this time the patient presented a deep-seated erythematous blush, with swelling over the nose and adjacent portions of the cheek. The tongue was swollen to several times its normal size. The tissues of the left ala nasi were missing. Symmetrically arranged on the thenar eminences were groups of deep-seated tender nodules. Later similar nodules appeared on both upper and lower extremities. Movement of the right wrist was difficult and painful.

At present the erythema and swelling of the face have disappeared, and an area of gangrene has developed, involving the right ala nasi and a small area in the labionasal fold. The swelling of the tongue has subsided, and an ulceration has appeared on the dorsum. The deep-seated, tender nodules on the thenar eminences and extremities are still present.

General physical examination revealed no adenopathy. The heart and lungs were essentially normal. Examination of the blood showed 4,000,000 erythrocytes and 28,650 leukocytes per cubic millimeter, with a normal differential count. Chemical examination of the urine revealed a 2 plus reaction for albumin and a trace of sugar. The microscopic examination showed a few erythrocytes and leukocytes and many granular casts.

Histologic examination showed that the epidermis was normal. There was a moderate degree of edema in the corium, with circumscribed mantles of infiltration about the blood vessels and sebaceous glands, consisting of loosely packed round cells. The biopsy specimen included but little subcutaneous fat, but it was here that the greatest inflammatory changes were seen, consisting of a diffuse infiltration of lymphocytes, histiocytes and a few plasma cells.

DISCUSSION

DR MAX S WIEN: Dr Finnerud and I saw this patient ten years ago in Cook County Hospital. At that time the diagnosis was erythema multiforme. She also had coin-sized patches on the trunk, compatible with a diagnosis of phenolphthalein eruption. Today she says she has not used any preparation in douches. This patient has erythema toxicum with severe local vascular allergy and associated necrosis, which may be produced by many different agents, such as drugs or infections.

DR C W FINNERUD: The whole process apparently is much more marked than when I saw the patient ten years ago. She has lost most of the nose since then. The disease appears to me to be an infectious process of internal origin. It certainly does not look much like erythema multiforme now.

DR PAUL A O'LEARY, Rochester, Minn.: The diagnosis of syphilis seems warranted. The tongue has the signs of syphilitic glossitis.

DR M R CARO: The biopsy specimen was taken from a lesion on the forearm. Unfortunately it cannot be of much help in making a diagnosis because most of the pathologic changes seem to lie deep in the fatty tissue, and the specimen was not cut deep enough to include them. The histologic picture, however, does not seem to be compatible with that of syphilis.

DR. DAVID LIEBERTHAL: I am strongly inclined to second the suggestion of Dr. O'Leary, to try antisyphilitic treatment in this case. I especially recommend using potassium iodide first.

DR. MINNIE PERLSTEIN: I saw this patient ten years ago when she had her first attack and again last week when she first entered the hospital. Ten years ago the picture was essentially the same as it is today except that the involvement was on the left side of the face. At that time she presented an involvement of the hands similar to that present today. On admission a week ago she presented an erysipelas-like swelling over the right cheek, extending from the angle of the mouth to the eyebrow, and she was acutely ill. A few days later painful erythematous plaques appeared diffusely scattered over the extremities, so that her legs could not be touched because of excruciating pain. Now she has no pain at all. The surprise to me now is to find that all the edema of the cheek has subsided and instead of a severe slough over the zygoma, which I believed would occur, there is but a small area of gangrene limited to the left ala nasi.

Lichen Planus Linearis. Presented by DR. M. H. EBERT.

P. V., a white girl aged 9 years, presents a linear eruption along the course of the left sciatic nerve. This appeared suddenly four weeks ago and does not itch. The lesion consists of a band 1 cm. wide made up of closely aggregated pinhead-sized flat papules, which were bright red when first seen.

Histologic examination showed: (1) lamellar hyperkeratosis; (2) hypergranulosis; (3) acanthosis; (4) edema of the rete, with fraying out of the lower cells into the infiltrate of the corium; (5) edema of the papillary layer, and (6) fairly well-defined round cell infiltration of the papillary and subpapillary layers.

DISCUSSION

DR. FRANCIS E. SENEAR: This case is one of those which Dr. Caro and I have recently been interested in. We have presented a number of cases before the society. Those we have been interested in recently have not been of lichen planus. There is often a great deal of difficulty in differentiating clinically lichen striatus from linear lichen planus. In this particular case, from a clinical standpoint, with the light just right one can see some lesions which are lichenoid in character, flattened, annular and brownish. In situations of that type I would say that the diagnosis ultimately has to rest on the microscopic picture. A point in favor of lichen striatus rather than lichen planus is that this condition has appeared and largely disappeared in six weeks' time. All authors point out that in dermatoses, such as lichen planus and psoriasis, the linear forms are more chronic. It has been our experience with the 8 cases of lichen striatus which we have had the opportunity to study that spontaneous involution in a period of a few weeks to a few months has been characteristic. In this particular case there is nothing in the clinical picture which might not be part of a slightly modified lichen planus.

DR. C. W. FINNERUD: I felt that the case histologically was one of lichen planus. There was hyperkeratosis, and a well defined infiltrate was present in one part of the section. Dr. Oppenheim did not think the condition could be lichen planus, because there was no sharp demarcation between the infiltrate and the basal layer of the epidermis. In my experience that very feature speaks for lichen planus rather than against it.

DR. M. R. CARO: I should like to disagree with the histologic diagnosis of lichen planus. The papillae were edematous; there was a loose cellular infiltrate that did not reach the epidermis, and there was no sharp line of demarcation at the lower border of the infiltrate. I thought a diagnosis of lichen striatus was more compatible with the condition in this case.

DR. E. A. OLIVER: This little girl presents a picture similar to that in 2 patients I have had under my care; one was a child and the other a man. In both the condition resembled linear lichen planus, and although no sections were taken, I did not believe it was that disease. Both patients responded readily to

treatment, the adult to fractional roentgen therapy and the child to ointments I feel that the condition was lichen striatus

DR M H EBERT If there must be a new dermatologic entity, I am pleased to have this type, one that disappears promptly with no treatment but with the dermatologist getting credit for doing good work When I first saw this girl, three weeks ago, the arrangement of the lesions was striking, the lesions closely resembling those of lichen planus The sudden onset impressed me A section was taken, and when she came back the next time her skin was almost clear, with practically no treatment except a soothing lotion I hesitated to present the case because she had no eruption as she did three weeks ago I thought the microscopic picture was of lichen planus There was hyperkeratosis and especially marked hypergranulosis The edema of the rete was what one sees in acute lichen planus The most striking feature was the fraying out of the lower cells into the infiltrate of the corium As Dr Caro says, the infiltrate is not as deep as in lichen planus, and the infiltrate in some places is about the blood vessels

Dermatofibrosarcoma Protuberans Presented by DR DAVID V OMENS and DR WALTER W TOBIN (by invitation)

T S, a Negro aged 42, states that thirty years ago he fell off a bicycle and scraped his left hip, which on healing retained a silver dollar-sized scar Eight years ago the scar thickened, and lumps began to form, which have increased in size and number There are no subjective symptoms

Examination discloses a palm-sized, freely movable area made up of scar tissue over the left trochanteric region, in which reddish and skin-colored nodules of varying size, some pedunculated, some sessile, are located Telangiectatic vessels are present over some of the nodules

The blood and the urine were normal A histologic examination of a nodule showed thinning of the epidermis, numerous large bundles of connective tissue and spindle cells

DISCUSSION

DR FRANCIS E SENEAR I think this patient presents a classic example of the disease

Pellagra and Myxedema Presented by DR THEODORE CORNBLET and DR DAVID COHEN (by invitation)

M K, a Lithuanian woman aged 47, presents an eruption on the hands, forearms, elbows and thighs of six months' duration At that time she began to have mental symptoms, such as hearing voices The skin began to turn brown and thick The patient was in Cook County Hospital in March 1939, where she remained until May, with the same symptoms and findings At that time nicotinic acid, 100 mg every four hours, was given, and she left the hospital free of symptoms

She now presents a brownish scaling eruption on the dorsa of the hands, extending to the forearms and wrists and also over the elbows and on the inner side of the thighs The areas are sharply demarcated The basal metabolic rate is —47 per cent

DISCUSSION

DR M J REUTER, Milwaukee I believe that the diagnosis of myxedema and pellagra is correct I suggest that the extensive hyperkeratosis in the groin is probably a feature of myxedema rather than of pellagra About eleven years ago, when working with Dr O'Leary, I had an opportunity to see a number of patients with myxedema It was not infrequent to find decided hyperkeratosis in the folds of the axilla and groin Incidentally, myxedema clinically does not appear until the basal metabolic rate approaches —38 or —40 per cent

DR THEODORE CORNBLET I never saw this type of eruption in a number of pellagrins that I examined before coming to Chicago At Cook County Hospital

I have been able to see several pellagrins who showed these well defined exudative and crusted lesions about the genitals and on the perineum. That picture was more evident last week than it is now. Treatment with nicotinic acid has caused great improvement.

Tuberculosis Verrucosa Cutis. Presented by DR. OLIVER S. ORMSBY and DR. WALTER W. TOBIN (by invitation).

M. B., a Negro aged 36, presents a verrucous, dirty grayish lesion on the left hand and a plaquelike scaly lesion made up of pea-sized nodules on the left shoulder and axilla.

The lesion on the hand began sixteen years ago, when the patient worked as a gutter in the Chicago stock yards. He states that while eviscerating an animal whose viscera were studded with small white lumps he accidentally scratched himself on the back of the left hand. Eighteen days later a sore developed in this area and enlarged. Three months later enlargement of the glands in the axilla developed, but the swelling went down, and shortly thereafter an eruption appeared on the shoulder.

The patient was seen first in 1936, at which time a test with a 1:1,000 dilution (0.1 cc.) of bovine tuberculin gave a positive reaction. A section taken in 1936 showed tremendous verrucous change, with an infiltrate of round and epithelioid cells.

DISCUSSION

DR. HENRY E. MICHELSON, Minneapolis: I think this case warrants discussion from many angles. First, to speculate on the course of events: This man was a gutter in an abattoir. He received an injury, and a lesion developed. Evidently he had an external inoculation, and the question is, Did a primary complex develop or did he have tuberculosis before and did a secondary inoculation develop? The fact that suppurating glands developed suggests a primary complex. The fact that his condition lingered so long and was benign makes one think that possibly the first lesion was a verrucous form of tuberculosis or a primary complex. As time went on, the lesions evidently became more lupoid in character and evidently became classic lupus vulgaris. It is well known that in any type of inoculation tuberculosis transition to lupus vulgaris is common.

DR. RUBEN NOMLAND, Iowa City: I agree with Dr. Michelson and should like to state that four years ago the lesions in the axilla were flat. The biopsy specimen taken from the axilla early in the course showed typical tuberculous structure and showed no verrucous areas, while a biopsy of tissue from the hand showed little tuberculous change but much hypertrophy of the epidermis.

DR. PAUL A. O'LEARY, Rochester, Minn.: My concept of this disease differs from that of my colleague. I consider this condition as occupationally acquired tuberculosis. It would have been easy for the patient to become infected with the bovine tubercle bacilli, for a tuberculous primary lesion to develop, with its resulting adenitis, and to be followed, by the process of contiguity, by tuberculosis verrucosa cutis. Whether this man had a previously existing Ghon tubercle is, I believe, of less importance than the type of organism with which he was inoculated. Inoculation tuberculosis, with its characteristic inoculation chancre, pipistem lymphangitis and adenitis, may subsequently manifest various types of cutaneous tuberculosis in the region of the inoculation site. Tuberculosis verrucosa cutis, lupus vulgaris and scrofuloderma have been observed on my service. I have searched unsuccessfully for other systemic manifestations of tuberculosis in our patients, because the literature contains reports of patients in whom miliary tuberculosis and erythema induratum develop subsequently.

DR. OLIVER S. ORMSBY: I think Drs. Michelson and O'Leary have expressed the same opinion. They agree that the case is one of inoculation tuberculosis. As Dr. O'Leary stated, the infection occurred on the dorsum of the hand and extended by way of the lymphatics up the arm and invaded the axillary glands. Scrofuloderma then developed, with secondary involvement of the overlying skin

producing a verrucous type of tuberculosis. In most of the cases of verrucous lupus that I have seen, general dissemination of the organism of tuberculosis occurred after an attack of some condition such as measles, with the development of numerous verrucous lesions, particularly on the extremities. In the present case the disease has remained comparatively local and is not of hematogenous nature.

DR J H MITCHELL. I think Dr Nomland will recall an old man we had some years ago with an inoculation of the verrucous type on the right wrist. His infection occurred while he was weighing sputum in the Municipal Tuberculosis Sanitarium. He had a little injury and the inoculation followed. The bacillus was presumably the human type and remained at the site of inoculation.

DR WALTER W TOBIN (by invitation). I have seen this man once since 1936 (that was in 1938), and at that time he had a positive reaction from a tuberculin test with bovine tubercle bacilli. I do not remember whether a roentgenogram of the lungs was made at that time.

Hidradenitis Suppurativa Presented by DR MAX S WIEN

H R J, a white police officer, aged 42, was first seen in November 1939, bedridden because of extreme weakness and exhaustion subsequent to chronic discharging abscesses in both axillae, with greater involvement of the right axilla and associated involvement of the perineum and the perianal area of four years' duration. The drainage was so intense that it caused great discomfort and prevented the patient from working. During this time he also noticed increased loss of strength and vigor and had a low grade fever, with a temperature between 99 and 100.4 F. In November 1930 examination of the blood revealed anemia, with slight increase in the leukocytes.

A clinical examination of the heart and lungs showed no abnormalities.

He was first seen at Billings Hospital in May 1939, with draining sinuses in the axillae, anal region and groin. The Frei test for lymphogranuloma venereum gave a negative reaction. Inoculation of tissue into guinea pigs showed no tuberculosis. Pus from one of the lesions showed only diphtheroid organisms. The Kolmer and Kahn reactions of the blood serum were negative, and the urine showed 3 plus reduction with Benedict's solution. Fasting blood sugar was usually low normal, but a sugar tolerance test revealed an abnormal curve. The fasting sugar was 93 mg at the beginning of the test, 208 mg after one-half hour, 283 mg at one hour, 175 mg at two hours and 99 mg per hundred cubic centimeters in three hours.

In view of the history and the results of laboratory tests, a diagnosis was made of hidradenitis axillaris which had extended to produce deep abscesses.

When first seen by me the patient presented the picture of cachexia and emaciation, with profuse thin purulent discharge from both axillae with greater involvement of the right. On extension of his right arm the axilla under tension revealed deep sulci, at the base of which were superficial ulcerations and pits that discharged pus. There was also thin purulent discharge in the perineal and scrotal area, with superficial ulceration and irregular margin to the border of the ulcers. On palpation of the margin of the right axilla, one could feel a definite boggy infiltrate that extended beyond the area of involvement and reminded one of the infiltration noted in erythema induratum (Bazin).

The right axilla is completely involved with red to reddish brown sulci with deep scarring approximating an irregular groove deep in the apex of the axilla. The entire area is moist with a thin seropurulent discharge that seems to well up from the depth of the irregular sulci produced by the scarring. There are also scarring and moderate discharge in the groin, of a less marked type, with cribriform scarring in the perineum and a linear band of irregular scarring radiating to the posterior aspect of the left thigh, which is dry and free of discharge. The patient's general condition is good, with considerable deposition of subcutaneous fat over the trunk and thighs, in contrast to the emaciation he presented when first seen.

SOCIETY TRANSACTIONS

DISCUSSION

DR. S. W. BECKER: I did not see the man today but I remember him. He was hospitalized at Albert Merritt Billings Hospital for some weeks, and the condition was studied by culture, microscopic examination and animal inoculation, and a tuberculous infection could not be demonstrated. It was considered hidradenitis of the type recently described by Brunsting (Brunsting, H. A.: *Hidradenitis Suppurativa*; Abscess of Apocrine Sweat Glands, *ARCH. DERMAT. & SYPH.* 39: 108 [Jan.] 1939) at the Mayo Clinic. He had severe hidradenitis of the axilla and groin.

DR. PAUL A. O'LEARY, Rochester, Minn.: I agree with the diagnosis of hidradenitis suppurativa. In my early experience with cases of this condition I felt that surgical intervention was contraindicated, a belief based on the fact, as I now see it in retrospect, that surgical drainage of the infected area tended to spread and prolong the course of the disease. It is now the practice to operate on these patients after a few weeks of preparatory treatment directed toward reducing the infection as much as possible. Rather than merely incising the infected nodules, the entire involved area in both axillas or in the groin with the underlying glands is now surgically removed, and a full thickness skin graft is done at the time of the excision. The use of the skin graft has materially decreased the period of healing; now six to eight weeks is required for recovery, whereas formerly as many months or more was necessary.

Another point of interest is the relation of hidradenitis suppurativa to peric folliculitis abscedens et suffodiens. Both diseases are the result of infection of the apocrine glands, of which there are many in the scalp. The onset of hidradenitis suppurativa following infection in the hand or forearm, followed by extension to the opposite axilla, the groin or the anal cleft or occasionally under large pendulous breasts, emphasizes the fact that the disease is systemic rather than local.

DR. MAX S. WIEN: When I first encountered this case of hidradenitis I was impressed with the resemblance of the infiltrate to that in erythema induratum (Bazin). In a discussion by Pollitzer (*ARCH. DERMAT. & SYPH.* 41:58 [Jan.] 1940) he stated that Philippon and he agreed on the essential features of certain remote cutaneous conditions and the group of tuberculids later described by Darier. The patient had a negative reaction to a von Pirquet test. He shows great improvement on a regimen of rest, fresh air and tonic therapy.

He was given roentgen therapy to the axillas, has gained 50 pounds (23 Kg.) since last September, is able to work again as a policeman, feels strong and is constantly gaining weight, as compared with his previous emaciated bedridden state.

HERBERT RATTNER, M.D., *President*

M. H. EBERT, M.D., *Secretary*

May 15, 1940

Erythema Figuratum Perstans. Presented by DR. DAVID V. OMENS and DR. WALTER W. TOBIN (by invitation).

B. K., a girl aged 11 years, states that two years ago a circular red patch appeared on the inner surface of each knee, the patch on the right knee still being present. About one year ago similar areas appeared on the thighs and on the back of the neck. They seem to fade at times but do not disappear. There is no itching.

The family and personal history are irrelevant.

Examination discloses palm-sized, annular and semicircular erythematous, scaling lesions on the nucha and the upper, inner aspects of the thighs and a circinate scaling patch above the right knee.

The urine and blood were normal. Histologic examination of one of the lesions on the thigh showed parakeratosis, moderate edema and an infiltrate of round cells mainly about the blood vessels.

DISCUSSION

DR C W FINNERUD I should like to ask how that diagnosis was arrived at Neurodermatitis is sometimes seen which has much this appearance I have seen neurodermatitis of the Vidal type in which circular segments were evident I wonder if this condition could not be of that class

DR S W BECKER I think this condition is a typical neurodermatitis of the Vidal type The configuration is a little unusual, but a bizarre type is possible I believe that this particular eruption lacks the rose red color and the central scaling of erythema figuratum perstans The lesions are somewhat like lichenified plaques

DR M E OBERMAYER I questioned the patient specifically as to the presence of pruritus, and she said that only mild itching was occasionally present Though there is a certain clinical resemblance of the condition to lichen simplex chronicus, I feel that this diagnosis cannot be made in the absence of pruritus

DR MAURICE OPPENHEIM (by invitation) Lichenified areas are absent It may be that the condition is some kind of erythema figuratum I thought of another disorder, xanthocrythroderma pityriasisformis of Radcliffe Crocker, because it is so yellow and has an irregular configuration, not round and not annular, and because the skin shows a fine flower-like desquamation I believe one must also think of a lesion belonging to the group of parapsoriasis I did not see the histologic sections, which would decide the question

A Case for Diagnosis (Hydroa Vacciniforme? Folliculitis Ulerythematosa Reticulata?). Presented by DR THEODORF CORNBLETT

Miss G M, a white woman aged 19, has had a disease of the skin of the face, neck and upper extremities off and on for the past four years The first episode began about Christmas time four years ago, lasted three or four weeks and subsided, with relief of all symptoms The following winter the cutaneous trouble recurred about Christmas and remained for six weeks The next episode was in August and September of 1939 Four weeks ago, following an appendectomy, the condition returned

At present there is an eruption on the scalp, face, neck and upper extremities and about the ankles On the upper extremities most of the lesions are on the extensor surfaces The lesions consist of small pinhead-sized to pea-sized crusts and excoriations There are pinhead-sized and slightly larger deep vesicles present as insets in a dry, chronic, diffusely inflamed skin The backs of the hands suggest remotely the changes associated with mild pellagra On the forehead especially there are follicular horny plugs There is a fine reticulated pigmentation present mostly on the face and a fine atrophic scarring paralleling the pigmenting process, all having a meshlike pattern The hyperpigmentation does not disappear between the episodes There is moderate to severe itching only during the active periods The general health is not affected, and the patient's diet has been and is adequate

Laboratory Tests—Urinalysis showed deep amber color, 1 plus reaction for albumin, no sugar and 1 red blood cell per high power field Examination of the blood showed 85 per cent hemoglobin and 4,450,000 red cells and 13,100 leukocytes per cubic millimeter, with a differential count of 83 per cent polymorphonuclear leukocytes, 8 per cent lymphocytes and 9 per cent monocytes, the nonprotein nitrogen amounted to 28 mg and the blood sugar to 107 mg per hundred cubic centimeters

The epidermis showed slight intracellular edema In one place there was thickening of the epidermis and intercellular edema Beneath this in the corium was a microscopic abscess containing many polymorphonuclear leukocytes, in addition to lymphocytes and histiocytes There were mantles of the same type of inflammatory infiltration about the blood vessels and some of the hair follicles The collagen fibers and elastic fibers were missing from the areas of infiltration but were intact elsewhere Perles' prussian blue reaction was negative for iron

DISCUSSION

DR. THEODORE CORNBLEET: I obtained a specimen of urine, but the quantity was insufficient to test chemically for porphyrin. Grossly the urine had a smoky appearance, somewhat in keeping with what one expects to find if much porphyrin is present.

NOTE.—The patient's urine was later examined for porphyrin; ten times the normal quantity was found in a twenty-four hour specimen.

DR. S. W. BECKER: This case is interesting, but it is difficult to make a definite diagnosis. The patient presents chiefly an excoriation, although she did have one bulla on the hand; this was a typical bulla and not the ordinary lesion seen in *hydroa aestivale*. The condition began when she was 16, which is the age at which acquired epidermolysis bullosa appears, though the face is an unusual location for these lesions. There is no history of the condition in other members of her family. It seemed to me she had linear crusts, as though there were excoriations rather than the type of lesion which would follow rupture of bullae.

DR. M. R. CARO: I thought that histologically there was hardly enough edema in the epidermis to fit in with the diagnosis of *hydroa vacciniforme*. The changes in the section were largely present in the corium and were of a type often seen in some varieties of pyogenic infection.

DR. OTTO H. FOERSTER, Milwaukee: The presence of distinct sensory abnormalities preceding the appearance of the eruption suggests that the condition is of the nature of *hydroa vacciniforme* and that photosensitivity may play a part in its production.

DR. THEODORE CORNBLEET: When I first saw this girl I looked carefully for the presence of vesicles or bullae, and none could be seen at that time. Several days later the patient was shown at the University of Illinois clinic, where several other staff members also did not find any vesicles. Several days after that there were definite vesicles present. Dr. Weber suggested the diagnosis of *hydroa vacciniforme*. Up to that time what impressed me a good deal was the reticulated atrophy present on the face and neck, together with a certain amount of pigmentation. I have an open mind about the final diagnosis in this case. It is noteworthy that a few days ago she was given an erythema dose of ultraviolet rays, and today erythema is present without any other changes.

A Case for Diagnosis (Parapsoriasis?). Presented by DR. M. H. EBERT and DR. A. H. SLEPYAN (by invitation).

The patient, a 72 year old scrap iron dealer, noted the onset of this eruption about five years ago. The lesions appeared progressively over the chest, the back, the lower part of the trunk and the sacral area, associated with only occasional itching.

Scattered over the entire back, on the extensor areas of the arms, in the axillas, over the sacrum and along the sides of the abdomen are discrete pinhead-sized to pea-sized areas of yellow brown atrophy, in places showing telangiectatic vessels. On the extensor surfaces of the arms are remnants of the scales that originally topped each lesion. The scales are yellowish brown, piled up and laminated and can be lifted off, leaving a smooth, glistening moist surface with occasional bleeding. On the scalp and face are numerous large comedos with considerable seborrhea. On the right leg the patient presents a large recurrent patch of stasis eczema of seven years' duration.

Examination of the blood showed 4,400,000 erythrocytes and 11,200 leukocytes per cubic millimeter, with a differential count of 52 per cent polymorphonuclear leukocytes, 12 per cent eosinophils, 8 per cent monocytes and 28 per cent lymphocytes. The Wassermann reaction of the blood was negative.

DR. OTTO H. FOERSTER, Milwaukee: My first impression of this unusual eruption was that it bore a close clinical resemblance to pityriasis lichenoides of subacute type. Further and more detailed examination led me to abandon that diagnosis and also that of leukaemia cutis, which was suggested to me more by

the microscopic picture, on hurried examination, than by the unusual eruption and other clinical features. The condition is new to me, and I have no diagnosis to offer.

DR MAURICE OPPENHEIM (by invitation) This interesting case reminds me of cases described at first by Kyrle under the name hyperkeratosis follicularis in cutem penetrans, but the histologic picture excludes such a diagnosis. The most prominent symptom of the microscopic slides is a broad band of uniform round cells which infiltrate compactly the papillary and subpapillary layer, sharply limited from the reticular layer. In some places one finds a subepithelial blister formation. This reminds me in a certain degree of a lymphatic leukemic infiltration. There is no decided hyperkeratosis or acanthosis. It is impossible for me to make a certain diagnosis in this case.

DR E. A. OLIVER I am glad that Dr. Ebert demonstrated this case today. It has been under observation at St. Luke's clinic for some months. The eruption has differed somewhat from the eruption present now. It suggested psoriasis and parapsoriasis of the lichenoid type. The scaling was much more evident than it is now, and the smaller lesions bled when the scales were removed. I could not arrive at a diagnosis.

DR C. W. FINNERUD I am extremely puzzled but equally interested. My first clinical impression was that the condition was an unusual form of parapsoriasis. What impressed me most when I examined the histologic section was the possibility of the condition's being leukemia. I believe that the so-called Senear-Usher syndrome must also be considered, in that there are features of seborrhea, lupus erythematosus and, microscopically at least, vesicles.

DR M. R. CARO I think there are certain clinical and histologic features about this case that suggest the diagnosis of atrophic lichen planus. Dr. Zeisler and I presented a case some years ago (Zeisler, E. P., and Caro, M. R. Lichen Planus with Fatty Infiltration, *ARCH. DERMAT. & SYPH.* 29:130 [Jan.] 1934) that was similar in many respects. In that case there were, in addition, some silvery streaks on the buccal mucosa and on the palate. The presence of keratotic follicular plugs in the skin can also be considered as being part of the picture of lichen planus, for such plugs were present in another case presented before this society (Caro, M. R. Lichen Planus, *ibid.* 28:725 [Nov.] 1933). The histologic picture in this case, while not pathognomonic, is also consistent with the diagnosis of atrophic lichen planus.

DR MINNIE PERLSTEIN I have seen this patient on numerous occasions since 1928. The last time I examined him was two years ago, at which time he presented no evidence of the eruption seen today. Since 1928 he has been hospitalized on two or three occasions because of chronic eczema on the legs and at times because of acute seborrheic dermatitis involving his chest and back. I at no time performed a biopsy, but the clinical picture seen today is entirely different from that shown at any previous time.

DR M. H. EBERT I am grateful for the discussion and for the various suggestions in the way of diagnoses. This case is unique, I have never seen a condition like it. I found it difficult to coordinate the clinical and histologic observations. When the patient was first seen the picture was considerably different from what it is now. The lesions that were described on his back were covered with crusts and presented a greasy appearance. The follicular lesions on the scalp and chest were about the same as today. My first diagnosis was Darier's disease. After picking off the scales I was not so certain. I was certain I had never seen a condition like it before. On looking at the histologic section this morning it occurred to me that there might be a possibility of lymphocytoma described by Epstein. Dr. Nomland had 2 or 3 cases of this at the Central Free Dispensary, benign tumors consisting of accumulations of lymphocytes and proliferation in situ. The lymphocytes were evidently preformed in that area. I also had a case of this kind which did not resemble this. It would be hard to fit that diagnosis in with the lesions in the peripheral vessels, the erythematous macules on the soft palate and the keratotic plugging of the hair follicles on the scalp.

I also considered Spiegler-Fendt sarcoma, but I have never heard of a tumor of that type breaking down and healing with this type of scar. I cannot throw any more light on the subject but simply speak of the various speculations. I think Dr. Finnerud's theory is a good one to follow. It would be worth while to consider lichen planus and seborrheic dermatitis, suggested by Dr. Caro. I do not know what more work can be done.

Acrodermatitis Chronica Atrophicans. Presented by DR. M. H. EBERT.

A. K., a married Ukrainian woman aged 42, complains of changes in the skin of the lower extremities of one and one-half years' duration. This condition started as a red patch on the right knee, spread to the remainder of the extremity and is associated with itching. The left extremity was involved two months later after an injury to the left knee.

The past history reveals that an operation was performed on the left side of the neck during infancy for an unknown condition. Five years ago a pelvic operation was performed following a miscarriage associated with severe metrorrhagia. She has three children living and well.

The process involves the lower extremities and extends on the buttocks and over the sacrum. The involved area is bluish red with atrophy. The superficial veins are prominent in all areas. The feet are cold and cyanotic, and there is considerable infiltration over the dorsa. The thighs present small shiny atrophic white areas alternating with violaceous-red areas, causing a mottled appearance. The skin over the right knee is infiltrated and arranged in transverse folds. Over the left patella at the site of a bruise which occurred in January 1940 there is a dark brown linear infiltrate covered with a silvery scale.

DISCUSSION

DR. S. ROTHMAN (by invitation): The history of this patient reveals early menopause, which is often found in patients with acrodermatitis chronica atrophicans. Although this fact has been mentioned in the literature several times its possible importance as regards the pathogenesis has not yet been investigated.

This disease seems to be rare in this country as compared with its incidence in central European states, where it is a rather common cutaneous disease.

DR. E. P. ZEISLER: I think it is worth while commenting on the scleroderma-like condition around the ankles and below the knees.

DR. MAURICE OPPENHEIM (by invitation): This eruption is typical of acrodermatitis atrophicans. There are two clinical features present which determine the final stage of this disease: first, the lipomatosis, which is distinct above the patellar region, where there are two pillow-like soft tumors which are due to the fact that the subcutaneous fatty tissue is growing after the degeneration of the tissue in the cutis (substitution *en vacuo*); second, the so-called pseudosclerodermatous changes of the skin on both legs, to which Dr. Ebert directed attention. A third final stage is acrofibromatosis, distinguished by the formation of fibromas at the extensor surfaces of the joints, this condition being absent in this case. The increase in connective tissue is caused by the degeneration of the elastic fibers, which inhibit the overgrowing of the connective tissue fibers.

An interesting fact is that so few cases of dermatitis atrophicans are observed in this country. Many cases have been observed in Vienna, and many more were published by Pautrier in Strasbourg.

DR. M. H. EBERT: I was pleased to hear Dr. Oppenheim's comments because I know he has done a great deal of work on this subject, particularly on the various changes that are associated with acrodermatitis, like new formations of elastic tissue and lipoidosis.

Argyria. Presented by DR. M. H. EBERT and DR. D. V. OMENS.

G. S., a 44 year old Polish man, has noticed a discoloration of the skin for the past six years. Fifteen years ago he underwent the first of six mastoid operations in five years, after which he used a 20 per cent solution of mild protein

silver as nose drops three or four times a day for nine years before he noticed a grayish discoloration of the skin of the face and neck. After that he continued using the solution only when the throat became dry, perhaps once a day or so up to the present time. Otherwise the patient has considered himself in good health.

Examination of the skin discloses a diffuse dark slate gray discoloration of the entire face, including the conjunctivas and the mucous membranes of the mouth. The color becomes gradually lighter on the neck, trunk, extremities and parts which have been covered by clothing. The nail beds are also slate gray.

DISCUSSION

DR A W STILIANS: I thought this case was interesting. The brown color, instead of the blue usually seen, I thought might be due to the fact that the skin is the type in which melanin develops easily.

DR THEODORE CORNBLET: One of my patients with argyria was studied by the hematologists. She showed evidence of a partial blockage of the reticulo-endothelial system. On looking over the literature I did not see any work done to corroborate this observation. It would be interesting to observe other patients with argyria to see if they, too, show such blockage.

Localized Solid Edema of the Extremities (Myxedema) Presented by DR FREDERICK R SCHMIDT

C K, a woman aged 43, is presented from the outpatient department of Grant Hospital. She entered the dermatologic clinic two weeks ago, complaining of pain in the legs with unsightly swelling. She had noticed swelling of the legs a year ago, but it had been intermittent. At that time she was nervous and was losing weight. The basal metabolic rate was +35 per cent. Thyroidectomy was performed in January 1940. A month ago the swelling of the legs became more noticeable. The basal metabolic rate on May 8 was -20 per cent.

The systolic blood pressure is 120 and the diastolic pressure 76. The cholesterol content of the blood is 220 mg per hundred cubic centimeters.

On the anterior surface of both tibiae, from the external malleoli a third of the way up the legs, are two well defined tawny, nonpitting, slightly reddened, elevated plaques. The skin is like pig skin in these areas. It is dry, waxy, translucent and firm. There is no evidence of inflammatory reaction.

DISCUSSION

DR L M WIEDER, Milwaukee: I think this clinical picture is usually thought of as being associated chiefly with hypothyroidism. The cutaneous changes were noted by the patient while he had a highly elevated basal metabolic rate. It is interesting that the condition became intensified after the thyroidectomy, and since then the basal metabolic rate has been lowered to -20 per cent.

DR FREDERICK R. SCHMIDT: In looking over the literature I ran across articles by Arzt (Arzt, L. *Med Klin* 30 49 [Jan 12] 1934) and O'Leary (O'Leary, P. A. *ARCH DERMAT & SYPH* 21 57 [Jan] 1930). Dr O'Leary published a series of 8 cases. A peculiar fact is that this particular type of circumscribed edema of the legs appears almost exclusively in patients with a metabolic rate above normal, in other words, in persons with hyperthyroidism. The other forms of myxedema—whether this case is one of true myxedema or not is not known—occur in persons with hypothyroidism.

A Case for Diagnosis (Infectious Granuloma?) Presented by DR M H EBERT

C T, a 59 year old married Negress, had multiple eruptions on her buttocks five years ago which she treated with heat and various ointments. In 1937 she had "big boils" in the same region and was treated surgically at a hospital, after

which she was symptom free for two years. In July 1939 she noticed some "bumps" developing about the anus, which have grown larger and are accompanied by a discharge necessitating the wearing of a pad. She has had no change in bowel habits and has only occasionally taken laxatives. The bowel movements have been well formed, soft and of the same size. She estimates that she has lost about 20 pounds (9 Kg.) in the past three months. There was no history of cancer in the family. Her husband had tuberculosis and at present is living and well.

Physical examination showed no abnormalities except signs of some emaciation. About the anus on both inner surfaces of the buttocks is a fungating granulomatous growth that bleeds easily. The one on the left side is about the size of a grapefruit, measuring 12 by 6 by 5 cm., with indurated base and multiple sinuses, while the mass on the right buttock is about the size of an apple, measuring 3 by 10 by 4 cm. On the left buttock a sharply circumscribed coin-sized lesion is present lateral to the granuloma.

A specimen for biopsy taken from the top of the granuloma by the intern in the surgical ward to which the patient was admitted was reported as a mucus-producing adenocarcinoma, probably metastatic, from the rectum.

A Frei test gave a negative reaction. Smears for Donovan bodies have been negative.

A specimen for biopsy taken from the base of the granuloma and examined by Dr. Caro fails to confirm the diagnosis of adenocarcinoma, and the histologic picture looks like that of an infectious granuloma.

DISCUSSION

DR. M. R. CARO: In the slide I examined I could find no evidence of carcinoma. The histologic picture was that of an infectious type of granuloma.

DR. M. H. EBERT: The clinical diagnosis in this case was granuloma inguinale from the first. Several attempts were made to find Donovan bodies, but they were unsuccessful. I still feel that that is the diagnosis. Some of the material was sent to the department of surgical pathology, and a report of adenocarcinoma was made, which led to the taking of another specimen for biopsy. There was no evidence of carcinoma. I think the condition is granuloma inguinale.

DR. MINNIE PERLSTEIN: In the course of a study of lymphogranuloma venereum, I performed many biopsies on various manifestations of this condition. Not infrequently, on examination of tissue from an ulcerated lesion, the report from the laboratory would be that the condition was a carcinomatous lesion. This observation is entirely in accord with Dr. Weidman's report of carcinoma-like changes occurring in a chronic ulcerative process.

Toxic Eruption Following Injections of Sodium Morrhuate. Presented by DR. M. R. CARO and DR. L. F. WEBER.

Miss M. B., aged 18, noticed an eruption seven days ago on the upper and lower extremities, face and trunk. She received five injections of sodium morrhuate for the obliteration of varicose veins of the legs. On April 26 she received two more injections of sodium morrhuate. One day later tenderness appeared at the site of injection and in the surrounding area. The right leg, the site of the injection, showed redness and edema. On May 8 the generalized eruption appeared; it is erythematous and papular. The condition is more severe on the upper and lower extremities. Subjective symptoms consist of burning and itching.

DISCUSSION

DR. S. W. BECKER: I have seen cutaneous eruptions follow the use of sodium morrhuate for obliteration of veins, but they were all allergic, never of this type.

DR. L. F. WEBER: Our experience has been limited to 2 patients. We have checked the records in the surgical department, and according to them the patients

have not had many reactions of any type. I know reports have been made of asthmatic attacks and urticarial attacks following injections of sodium morrhuate. In both of our patients the causes have been similar. There was a severe reaction at the site of injection, and within a day or two a generalized toxic eruption appeared. In the other case the condition ran its course in twelve days. This patient has made some improvement in the last two days. I think in another few days the eruption will be practically cleared up. I have searched the literature for reports of toxic eruptions following sodium morrhuate but so far have not found any. I was also questioned about what substance or what part of the sodium morrhuate was the damaging agent. I am unable to answer that. So far I am still of the opinion that the reaction in the leg was a thrombophlebitis. It is important to know the causation of the toxic eruption.

DR M E OBERMAYER To make certain that the condition is a toxic eruption from sodium morrhuate it might be worth while to continue the injections with monolthanolamine oleate instead. The latter supposedly contains no protein, and if injections with that compound are unaccompanied by toxic symptoms it would seem fair evidence that the proteins contained in sodium morrhuate were responsible for the eruption. However, in my experience, even monolate may occasionally cause toxic eruptions, though of a milder degree.

DR L F WEBER I have felt that this toxic reaction has not pursued the course of a protein reaction. Both of the patients have had five or six injections. I thought that was not the usual course of a protein reaction.

DR FREDERICK R SCHMIDT A condition similar to this occurred at Grant Hospital. The curious thing is that the eruption was not limited to the legs but involved the face and neck, with little on the trunk. I wonder if there is a factor of sunlight present, for the lesions in that case were limited to the exposed skin.

DR L F WEBER The condition was more noticeable on the face two days ago than today.

Adenoma Sebaceum and Tuberous Sclerosis Presented by **DR MINNIE PERLSTEIN**

J V, a boy aged 12½ years, presents the following history. He was apparently developing normally until he was 18 months of age, when he had a convulsion associated with a right hemiplegia. After this he seemed duller than before and did not begin to speak until he was 3 years of age. He had a second convulsion at 6 years of age and since then has had attacks about every six to eight weeks. His mental condition has been slowly regressing.

On examination, he appears dull but cooperative. Scattered over the flush areas of the face are discrete, isolated and grouped pinpoint-sized to match head-sized bright red, firm papules. There are small depigmented areas scattered over the body, with numerous subcutaneous fibrous nodules located especially over the sacral area. The physical examination otherwise gave essentially negative results except that on ophthalmologic examination definite sclerosis of the fundus of the right eye was observed. His intelligence quotient was 67, with marked scatter.

Encephalography, by Dr Meyer Perlstein, showed normal cortical markings, dilated lateral ventricles, especially on the left side, deviation of the septum pellucidum to the right and a calcified area at the base of the left lateral ventricle in the choroid plexus. The encephalographic diagnosis was left internal hydrocephalus, a calcified or sclerotic patch was observed in the left choroid plexus, approximately 1 inch (2.5 cm) above the sella turcica and to the left of the midline. The sella was unchanged. Electroencephalography showed abnormal waves in the left motor area.

In summary, this 12 year old boy presents the syndrome epiloia, which includes epilepsy, due to sclerosis of the choroid plexus in the left lateral ventricle, adenoma sebaceum, associated with vitiligo and neurofibromas, and mental deterioration.

DISCUSSION

DR. OTTO H. FOERSTER, Milwaukee: The association of tuberous sclerosis and epilepsy has been known for many years. About thirty years ago, in company with a neurologist, Dr. N. S. Yawger of Philadelphia, I examined a large number of inmates of an epileptic colony and found that some of them had more or less well developed adenoma sebaceum. A number of these patients died some years later, and I was informed by the neurologist that autopsies on several with adenoma sebaceum had disclosed the presence of tuberous sclerosis.

DR. MINNIE PERLSTEIN: This boy presents the typical picture of epiloia; namely epilepsy, mental deterioration and eruptions of the adenoma sebaceum type. His mental age is roughly about $6\frac{1}{2}$ years, and he is in the sixth grade of a school for mentally deficient children. His mentality is gradually decreasing, a fact of which he is aware. There is no history of any familial tendency in this direction. The other three children in the family are apparently normal. In addition to the sclerotic patches seen over the sacral area and those seen on encephalographic examination, there is also evidence of a sclerotic patch in the retina.

NEW YORK DERMATOLOGICAL SOCIETY

FRANK C. COMBES, M.D., *President*

J. GARDNER HOPKINS, M.D., *Secretary*

April 23, 1940

A Case for Diagnosis (Circumscribed Scleroderma of the Cheek?). Presented by DR. FRED WISE.

Dr. A., a physician aged 32, is in good general health. The past personal history is irrelevant. About six weeks ago he noted an area of baldness on the bearded region of the right cheek. This area is oval, about 2 inches (5 cm.) long and $1\frac{1}{2}$ inches (4 cm.) broad, with fairly well defined borders. The condition resembles alopecia areata, but palpation discloses that the involved portion of the cheek not only is devoid of hair but is indurated to a slight degree. The patient states that the loss of hair preceded the onset of the induration. Subjective symptoms are absent. About nine months ago the patient had extensive dental work done on both sides of the mouth, requiring from six to eight roentgenograms. There are no signs of dermatitis, dryness of the skin or other evidences of excessive exposure to roentgen rays on either cheek, nor has the patient noted a previously existing inflammation of the skin of the face. No treatment has as yet been prescribed.

DISCUSSION

DR. HOWARD FOX: It is difficult to make a diagnosis in this case. The patient presents an obvious patch of alopecia areata, which on manipulation apparently shows an urticarial reaction. It does not have the color, consistency or lilac border of morphea.

DR. EUGENE F. TRAUB: I agree essentially with what Dr. Fox said. There is certainly no glazing of the skin. The skin does not look generally infiltrated over the whole area, nor does it look thinned or atrophic.

DR. A. BENSON CANNON: I think the case is one of amyloid degeneration or, possibly, of superficial sarcoid. The lateral and lower parts of the lesion are infiltrated and raised, and one can make out the lobulated structure in the infiltrated portion, somewhat resembling the shape of a four leaf clover. I think that a biopsy will be necessary in order to establish a diagnosis.

DR. R. H. RULISON: I am wondering whether this condition may not be just alopecia areata which perhaps has been self treated, resulting in some inflammatory reaction.

DR FRED WISE The fact that the alopecia preceded the infiltration is a puzzling feature of the condition

A Case for Diagnosis (Capillary Nevus?). Presented by DR J GARDNER HOPKINS

F Z, a girl aged 3½ months, presented no abnormality at birth. When she was 2 months old a dark red area suggesting hemorrhage was noted. The left cubital fold and the left hand were deeply cyanotic and became normal in color when the arm was held extended. She was seen again at the age of 3 months. The red area at the elbow was more evident, and both lower extremities became cyanotic when she cried. Ten days later an irregular dusky appearance was noted on the upper anterior portion of the left side of the chest, in the left axilla and on the outer surface of the left arm. The color in all of these areas disappears on pressure, and the dilated vessels fill slowly when pressure is released. Otherwise there seems to be little that is unusual about the lesion.

DISCUSSION

DR EUGENE F TRAUB This condition is probably a naevus flammeus, just beginning. I should leave it alone.

DR A BENSON CANNON I also think that the condition is a naevus flammeus and not sufficiently pronounced to warrant treatment of any sort, but I believe that blistering doses of ultraviolet radiation would be my choice of treatment should the parents want the blemish removed.

DR HOWARD FOX I agree with the diagnosis but consider it unusual for a naevus flammeus to make its appearance as late as two months after birth. As the treatment of naevus flammeus is always difficult and usually unsatisfactory, I advise that none be given in this case.

DR FRED WISE I also agree with the diagnosis, and I should be especially concerned about possible involvement of deeper structures.

Extensive Lupus Vulgaris Treated by Surgical Methods Presented by DR EUGENE F TRAUB

H M, a woman aged 46, suffered from extensive lupus vulgaris which involved the greater portion of the scalp, scattered areas on the lower part of the abdomen, the labia and the perineal area, extending posteriorly to the buttocks and about the rectum. In addition to the cutaneous lesions, the patient has pulmonary tuberculosis, as demonstrated by roentgenograms. She does not have a cough or other clinical evidence of this disease, however.

The patient has received a great deal of treatment, without any success. In 1938 extensive surgical excisions with plastic repair were made by Dr Herbert Willy Meyer. The results have been excellent, and there have been no recurrences of the condition.

DISCUSSION

DR HERBERT WILLY MEYER (by invitation) This case is interesting from several points of view. One is, as Dr Traub stated, that he did not believe dermatologic treatment would be of any further avail. The patient had been at the Leahy Clinic in Boston and at several other institutions.

I first excised an area on the forearm and performed a Thiersch graft, taking the skin from the thigh. Microscopic examination of the tissue removed showed typical lupus vulgaris. Having had good results with this, I next excised an extensive area on the forehead and performed a Thiersch graft. When that wound had healed, a few weeks later, I excised all of the remainder of the scalp which was involved over the bony part of the skull, and another Thiersch graft was done. A few weeks later I excised the rest of the area on the back of the neck and grafted that also. The grafts healed well.

The patient had an extensive area on the buttocks and was unable to sit because of painful ulcerations over the sacrum. I therefore excised this area right down

to the fascia over the muscles and up to the mucous membrane of the anus. In order to give her some soft tissue on which to sit, I made parallel incisions to the excised wound and undermined the skin of the buttocks on each side, sliding these flaps over to the midline of the exposed area and leaving defects on either side, which were covered with skin grafts. I sutured the mucous membrane of the anal margin to the flaps. There was a little difficulty in healing because of a collection of fluid, but healing did take place, and she is now able to sit in comfort. In fact, she has just returned from a motor trip to California.

The patient also had a rather large area on the lower part of the abdomen, down to the labia majora on either side of the vagina. I excised this area, including the labia majora, sutured the latter and repaired the defect with skin grafts. All of this work was not done at the same time. It was done in stages. I took two crops of skin grafts from the thigh. For the work on the lower part of the abdomen I took the skin grafts from the same thigh. There was also an extensive lesion on the ear. I excised the skin of the ear down to the cartilage and performed another Thiersch graft. These grafts were split skin grafts. This work was done in 1938. There were four separate operations. The patient was in the hospital from March to May 1939 and again from October to January. There has been no recurrence in the scars. There is one small new spot present now on the abdomen but not in the scarred areas.

DR. HOWARD FOX: The result is excellent, as two years has elapsed without any sign of recurrence. I have long considered that surgical excision was perhaps the best method of treating small patches of lupus vulgaris. In this case the surgeon is to be congratulated for his courage and skill in operating on such extensive and numerous areas. The results are most encouraging, in view of the shameful neglect or, at best, the poor treatment of lupus vulgaris in this country. I know of no Finsen institute in the United States similar to the many that exist in Europe. The reason is perhaps the comparatively small incidence of the disease in this country. One feature of lupus vulgaris which makes a radical cure difficult is the frequent involvement of the mucous membranes. That was fortunately absent in this case. As lupus vulgaris does not often occur coincidentally with pulmonary tuberculosis, I should like to ask Dr. Traub whether the roentgenogram of the chest indicated active tuberculosis in the opinion of the roentgenologist.

DR. HERBERT WILLY MEYER: Dr. Thorburn saw this woman in consultation. She has no cough and raises no sputum. Her temperature has not been elevated. She has no clinical signs of a pulmonary lesion, although the lesion is evident on the roentgenogram. All of the pathologic specimens were examined at the Lenox Hill Hospital, and all showed typical lupus vulgaris.

DR. J. GARDNER HOPKINS: Heretofore in undertaking operative removal of areas of lupus, there has been fear of infection in the scar. It is extremely interesting that the surgeon was able to do such extensive removal without the patient's incurring any infection.

DR. PAUL E. BECHET: I presented a patient before the Manhattan Dermatologic Society this month (ARCH. DERMAT. & SYPH., to be published) with extensive tuberculosis cutis of one buttock. The disease had been present for approximately fifteen years. A large section of the lesion had been excised at Mount Sinai Hospital six years previously, and there has been no recurrence in the excised area. The scar is smooth and not at all unsightly. The diseased areas not excised have extended until a considerable part of the buttock is involved.

Lupus vulgaris in certain instances can be just as mutilating and as malignant as carcinoma, and it should be treated just as vigorously. I have observed several cases in which the disease was extensive and spread to two and three times its former size after five or eight years of local cauterization with mild escharotics, roentgenotherapy, salt-free diets and timid electrodesiccation. The excellent results of surgical excision and skin grafting as demonstrated in Dr. Traub's case bring

to my mind the fact that this method of treatment offers in certain instances—depending on the severity, location and degree of the condition—such apparent permanence of cure as to warrant its more frequent use

DR EUGENE F TRAUB It is not known how rapidly the pulmonary tuberculosis is spreading, because the patient has no clinical symptoms. An active process seems to be going on, however, because since the first roentgenogram was taken two years ago there has been definite advancement in the condition, according to the roentgenogram taken a few days ago. I presented this case because I have several times heard it said that surgical therapy is not particularly good in cases like this because of the possibility of recurrence in the scars. I know this method has been practiced at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, and I have followed many of the cases for twenty years, I remember only 1 or 2 in which there were recurrences, provided the excision was properly done. In a number of cases ears have been involved, and new ears have been constructed. I have several patients now being treated for new spots on the body, but the newly constructed ears are doing well, with no local recurrence. One of the most interesting points to me was to find out whether lupus vulgaris might not develop in the area from which the grafts were taken. The area on this patient's thigh which had been used over and over again was smooth and showed no signs of tuberculosis. I think Dr Meyer is particularly to be congratulated for the way in which he handled the area around the anus and buttocks. One would ordinarily expect lupus vulgaris to be dry and nonulcerative, with the skin unbroken. However, she had a large number of abscesses on the buttocks where the skin had broken down. I treated her with a great many bland remedies for a while, thinking that the ulcerated area was so extensive it might heal and cure itself. However, that did not occur. Dr Meyer had, therefore, not only to excise a tremendous area of lupus vulgaris but to go deep to excise the abscesses. The idea of moving the skin from the lateral side of the buttocks over to the midline to cover the bad area and graft the sides thus left exposed was a brilliant one. It was done so that she would be able to sit comfortably and defecate without danger of contamination of newly grafted skin.

Pruritus (Icterus), Carcinoma of the Gallbladder Presented by **DR A BENSON CANNON**

E L, a widow aged 64, consulted me on April 10, 1940, complaining of severe generalized itching with the formation of nodules. Her family history is not significant. Her husband died at the age of 55, of an unknown cause. She has a daughter, aged 40, who is partially paralyzed. She has had no miscarriages. At the age of 48, sixteen years ago, the patient was treated surgically for fibroid tumors of the uterus. The onset of her present condition occurred six months ago, with severe generalized itching which was most pronounced over the lower extremities. Itching caused loss of sleep and nervousness. Her physician gave her injections of a calcium compound intravenously and local remedies for relief of the itching, as well as some "pink tablets" to help her sleep. She has lost about 20 pounds (9 Kg) in weight in the past four to five months and tires more easily than usual. In the last two or three months she has noticed many red nodules on the skin, especially on that of the extremities. Small, red, intensely itching papules appear in the skin. She has had no other treatment.

Examination shows a thin, pale woman who appears much younger than she is. Her complexion is sallow and slightly yellowish. The scleras are white with a yellowish tinge, the mucous membranes are pale, and the tongue is smooth, shiny and yellowish red. The skin of the body and extremities is yellowish brown and muddy, giving a mottled appearance with darker and lighter areas. There are many superficial excoriations especially evident on the extremities, with pea-sized whitish scars surrounded by a pigmented margin. Some of the recent scars have infiltrated edges. There is an occasional brownish red, split pea-sized, conical papule surrounded by a firm, hard infiltration that is felt but not visible. All the superficial glands are palpable, the size of a small pea, firm and freely movable.

There has been a pronounced loss of hair in the last four to five weeks, with almost total alopecia in back and around the sides of the scalp. Both the liver and the spleen are palpable. The liver is not much enlarged. In the right upper quadrant of the abdomen is a noticeable bulging. Just to the right of and above the umbilicus is a sharply demarcated, hard, irregularly shaped mass that is movable but is apparently attached to some deeper organ, being situated over the region of the gallbladder or the head of the pancreas. The mass is the size of an orange. Percussion over this mass gives a note of flatness. The heart is not enlarged. A short systolic murmur is heard over the precordium and is loudest over the aortic area. The blood pressure is 142 systolic and 78 diastolic. Roentgenograms of the lungs, the mediastinum and the gastrointestinal tract were all normal. A large mass was seen, apparently attached to the head of the pancreas, with involvement of the gallbladder. The liver was also enlarged. The roentgenologic diagnosis was probable primary carcinoma of the pancreas. The Wassermann, Kahn and Hinton tests gave negative results. The results of chemical examination of the blood were normal. The icteric index was 18. Urinalysis showed a trace of albumin and 25 to 50 white blood cells, while the test for the bile gave positive results. A blood count showed 2,650,000 erythrocytes per cubic millimeter, with 40 per cent hemoglobin and 11,500 leukocytes per cubic millimeter, with 70 per cent polymorphonuclear leukocytes, 22 per cent lymphocytes, 6 per cent monocytes and 2 per cent eosinophils.

DISCUSSION

DR. R. H. RULISON: I agree with the diagnosis. I think the patient has a malignant growth in the abdomen, with secondary cutaneous changes.

DR. HOWARD FOX: I agree that the patient probably has a visceral carcinoma, but I did not see any clinical evidence of jaundice. The scleras were apparently normal, as I compared their color with that of the scleras of some of the members of the society. There was a generalized pigmentation, which I thought was probably due to the malignant condition. The increase of bile in the blood, however, might well have accounted for the itching.

DR. EUGENE F. TRAUB: I thought this patient had clinical jaundice. While it is not very evident in the scleras perhaps, even the mucous membranes of the mouth showed it well, particularly the tongue. I think the carcinoma is most likely in the head of the pancreas and not in the gallbladder. That is the usual location with this type of syndrome.

DR. J. GARDNER HOPKINS: The patient appears to be jaundiced and probably has been for a long time, but the jaundice is rather mild. Would mild jaundice of long duration account for the pruritus? I suspect it would. Or could the pruritus be perhaps accounted for by the atrophic changes in the skin?

DR. PAUL E. BECHET: The patient may have an icteroid pruritus, but there is not much corroborative evidence of it. She presents no definite symptoms of jaundice. The lesions are most noticeable on the lower part of the legs, where they present scooped out excoriations and not scratch marks. I would class the eruption as neurotic excoriations in a woman who has a carcinoma rather than as generalized pruritus due to icterus.

DR. FRANK C. COMBES: I agree that the patient has some jaundice and probably has some pruritus. Patients with pruritus due to jaundice do not usually scratch as this woman does. There may be some neurotic factor present. She has dug out punctate areas. Patients with jaundice tend to scratch with the palm, as do persons with urticaria, rather than with the nails.

DR. A. BENSON CANNON: The inference that the abdominal tumor is responsible for all the symptoms cannot be evaded. The itching was the primary symptom, followed by the appearance of urticarial papules, excoriation, scarring and pigmentation and infiltration around the scars. It is not remarkable to encounter patients with severe jaundice but no itching and still others with no clinical evidence of jaundice (only a high icteric index) but with intense pruritus.

A Case for Diagnosis (Leukemid?) Presented by DR EUGENE F TRAUB.

H G, a woman aged 49, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, complains of an eruption which began a little over three months ago on the arms, neck and face and suggests an early stage of dermatitis of the contact type. It was thought that possibly the eruption was due to dye in one of her dresses, a woolen sweater or some other material contacted by her. The eruption on the face and neck cleared up, but the eruption on the arms has continued, it has itched intensely, and the skin is now thickened and lichenified. In addition, in the past three or four weeks, an entirely new type of papular eruption has developed, confined largely to the thighs and both legs. These papules have a definite infiltrated feel, are a little darker yellowish brown than the normal color of the skin and are discrete, with no tendency to confluence. They do not suggest a lichen planus papule in their size, location in the skin or color. There is no scaling.

Histologic examination of a papule showed the following features. In the center of the section was a small area in which the epidermis was acanthotic and platelike. The lower border was edematous, and in part the basal cell margin was absent. The granular and horny layers were present. In the upper part of the cutis there was a moderate bandlike cellular infiltrate extending up to the epidermis and composed chiefly of small round cells. Incidentally, beneath the lesion was a neurofibroma which was composed of bundles of fibrous tissue throughout which there was a diffuse infiltrate of fibroblasts.

Examination of the urine for arsenic and lead gave negative results. A complete blood count showed a severe secondary anemia, as manifested by anisocytosis and a moderate degree of poikilocytosis, with considerable achromia and some polychromatophilia.

DISCUSSION

DR FRED WISE. I do not think that the eruption is one of lichen planus. The eruption resembles leukemid, although I would not have thought of that condition unless I had some additional evidence to bring it to my mind. As to the lesions on the arms, I believe that the constitutional disturbance, whatever it is, caused the scaling and hyperpigmentation. They are probably two different manifestations of the same disease.

DR A BENSON CANNON. I agree with Dr Wise that this condition is probably leukemid, although I am not at all positive. I believe that the patient should have a more thorough investigation before a definite opinion of the eruption is given.

DR R H RULISON. I agree with Dr Wise that the trouble has some primary lesion which is probably internal, and I think the dissimilar cutaneous lesions are probably from the same source. However, what that is I do not know.

DR J FRANK FRASER. I agree with the views expressed by Dr Wise but should like to add that in my opinion the histologic picture harmonizes more with the clinical diagnosis of leukemid than with that of lichen planus.

DR EUGENE F TRAUB. When this patient first came in I thought she had a most peculiar discoloration of the skin of the face and of the body generally. The skin has a peculiar cast, so much so that I thought of a possible icterus, but that was excluded. Then the question arose of secondary or pernicious anemia. The blood count, of course, is that of a peculiar type of secondary anemia. I think that there is some type of peculiar constitutional disease from which she is suffering and that the cutaneous lesions are secondary to that. I could think only of leukemia, but I have nothing to substantiate that diagnosis. I sent that diagnosis with the specimens to Dr Satenstein. He did not comment on it but made a diagnosis of early lichen planus, which I do not think this case suggests clinically. Dr Fraser, I believe, stated the opinion that the histologic picture is not inconsistent with a diagnosis of leukaemia cutis or leukemid.

A Case for Diagnosis (Mycosis Fungoides? Leukemid? Hodgkin's Disease of the Skin?). Presented by DR. FRED WISE.

M. F., a pharmacist aged 28, born in England, a patient of Dr. Jack Wolf, was first examined on July 12, 1934, complaining of an eruption of three years' duration, which began as a hard red plaque the size of a nickel on the anterior part of the chest. Another similar lesion appeared on the midportion of the back, and then tumors gradually appeared on other parts of the back, on the right thigh and on the scalp. The eruption was asymptomatic. Three months ago he had a peritonsillar abscess which was incised and drained. His history is otherwise insignificant.

The eruption at this time consists of lesions spread widely over the chest and back, a few on the frontoparietal aspect of the scalp and one on the right hip, the remainder of the body remaining free. On the back the lesions are small and coin shaped, erythematous, with a faint bluish tinge, elevated above the skin, definitely circumscribed and firm on palpation. In several areas confluence has occurred, with the formation of variously sized, irregular, more elevated plaques, especially over the left scapula. There are no visible or palpable axillary or inguinal nodes, nor can the spleen be felt.

Histologic study, on July 12, 1934, of tissue from a lesion on the back, showed the following features: Scattered throughout the cutis, predominantly in the middle and deeper zones, were irregular foci of cellular infiltration. In some of these areas were small thin-walled vessels. In the upper part of the cutis there was a sparse perivascular cellular infiltration. The elements of the infiltration in the middle and deeper parts of the cutis were predominantly of the small lymphocyte variety. The chromatin fibers and granules of the nuclei could be made out, and in some of the areas a small round area of protoplasm was noted. Mixed among these cells were some nuclei of the endothelial variety. The blood vessels when noted were almost occluded by swollen nuclei. There was no special arrangement of these cells, with mitotic figures or any special changes of the surrounding cutis. The observations in this specimen appeared similar to those noted in the lymphadenoses and similar conditions.

The Wassermann reaction of the blood was negative. A blood count showed 90 per cent hemoglobin and 4,500,000 erythrocytes and 8,800 leukocytes per cubic millimeter, with a differential count of 37 per cent polymorphonuclear leukocytes, 52 per cent lymphocytes, 3 per cent large mononuclear leukocytes, 5 per cent eosinophils, 1 per cent basophils and 2 per cent myelocytes.

Therapy consisted of a total of seven skin units (2,100 r) of roentgen rays over the affected areas during five months. No single lesion received over two skin units, however, and all roentgen rays were unfiltered. The lesions responded favorably to this therapy, but the patient failed to return. He was not seen again until April 17, 1940, after having received interim roentgen therapy from another physician. At this time he presented on the anterior wall of the chest a deep ulcer with an elevated, cartilaginous-like border, oval, approximately 5 by 4 inches (13 by 10 cm.) in diameter. Its base was ulcerated, moist and granular in appearance. The lesion was sharply margined. Adenopathy was not more pronounced than in a normal person except that the epitrochlear glands were pea sized, hard and difficult to palpate.

Microscopic examination showed a tremendous cellular infiltrate, partly focal and partly diffuse. The cells were all large, with large oval hypochromatic nuclei and definite cell bodies. Some of the cells were multinucleated, suggesting Sternberg cells. There were some mitotic figures. At another edge of the section the vessels were dilated, and about them was a definite cellular infiltrate composed of small round cells. The epidermis showed no important changes. The histologic diagnosis was lymphoblastoma, suggestive of Hodgkin's disease.

The blood count at this time showed 90 per cent hemoglobin and 5,350,000 erythrocytes and 8,900 leukocytes per cubic millimeter, with a differential count of 5 per cent nonsegmented and 61 per cent segmented polymorphonuclear leuko-

cytes, 25 per cent lymphocytes, 4 per cent monocytes and 5 per cent eosinophils. The platelet count was 250,000 per cubic millimeter. A roentgenogram of the chest was normal.

DISCUSSION

DR J FRANK FRASER Because of the apparent origin of the lesion in the skin I should not entertain the diagnosis of lymphoid leukaemia cutis. The fundamental changes in that disease begin in lymphoid tissue. There is no evidence of involvement of the lymph nodes in this case. On the other hand, the fact that the lesion is in the true skin and the gross appearance are suggestive of mycosis fungoides. Mycosis fungoides is primarily a cutaneous disease, and the occurrence of adenopathy is a secondary phenomenon and theoretically may never supervene. From a brief examination of the slide presented, I feel that this case should be recorded as an example of mycosis fungoides of the d'emblee type.

DR EUGENE F TRAUB From clinical inspection I should say that the lesion on the abdomen presents about as classic a picture of what is called mycosis fungoides as anything could. It is a crescentic or horseshoe-shaped lesion and in a location, strangely enough, where one is particularly accustomed to see this type of lesion. From the points mentioned by Dr Fraser and from the fact that the patient is still alive and well nine years after the first appearance of the condition, I should say that the disease is a slowly progressive d'emblee type of mycosis fungoides. I recall a patient with an identical lesion on the abdomen, in whom a great many of these lesions developed as time went on. They all disappeared as a result of roentgenotherapy and were replaced by a large number of tumors which were histologically lymphosarcoma. I think the picture both clinically and microscopically may be definite in these cases.

DR HANS J SCHWARTZ I agree with the clinical diagnosis of mycosis fungoides.

DR A BENSON CANNON I, too, thought mycosis fungoides the most likely diagnosis, but one should not lose sight of the possibility of the lesion's being sarcoma.

DR GEORGE C ANDREWS I agree with Dr Traub's conception of the case.

DR J GARDNER HOPKINS I think the condition is mycosis fungoides. I should like to ask Dr Fraser if he did not think that the cells were larger than those ordinarily seen in leukemia. The cells also seemed more uniform than they are usually in mycosis fungoides. Is the histologic picture of mycosis fungoides with tumors at the onset a little different perhaps from that of the typical example of the disease in the third stage?

DR J FRANK FRASER In answer to Dr Hopkins' question, the cells in this section are reticular and longer or larger than the lymphoid cell of lymphatic leukemia.

DR R H RULISON Would there be any advantage in making a complete excision of this lesion and then grafting skin?

DR J FRANK FRASER Surgical excision is contraindicated. Roentgenotherapy is preferable.

DR PAUL E BECHET I agree with those who feel that the condition in this case is mycosis fungoides. The lesion on the back which is not ulcerated is infiltrated and suggests mycosis fungoides. Another point which is in favor of that diagnosis is that the lesions were particularly sensitive to roentgenotherapy.

DR HOWARD FOX The former lesions on the back and the one now present on the abdomen are probably the same disease. From the clinical appearance and from the histologic and serologic studies that have been made, one can exclude syphilis, tuberculosis, carcinoma and sarcoid. The probable diagnosis of lymphoblastoma remains by exclusion. The extreme sensitivity of the former lesions on the back to roentgen rays favors this diagnosis. I also understand that the lesion on the abdomen has probably received an inadequate amount of roentgen rays. Mycosis fungoides is, I think, the most likely diagnosis.

DR. GEORGE C. ANDREWS: Although mycosis fungoides is usually regarded as a systemic disease, I think, as Dr. Fraser said, that it primarily begins in the skin and that if one treats the original d'emblée lesion effectively, there is a chance to stop the process. I base that conclusion on a case similar to the one mentioned by Dr. Fraser. The patient had a d'emblée type of mycosis fungoides on the abdomen. The condition was seen by Dr. Satenstein and others and definitely accepted as such. He was presented before the Manhattan Dermatologic Society (ARCH. DERMAT. & SYPH. 33:182 [Jan.] 1936). I treated the ulcer with a heavy dose (8 erythema doses) of roentgen rays, filtered through 3 mm. of aluminum. Atrophy developed at the site of the lesion. The lesion at the time of treatment was a large ulcerated tumor, measuring about 4 inches (10 cm.) in diameter, and it was the only lesion present. He remained entirely free from lesions for eight years, and then pruritic infiltrated patches developed on the thighs.

DR. FRED WISE: I assume that all dermatologists have encountered so-called borderline conditions like this one, a definite diagnosis of which is not arrived at either with the aid of the microscope or by any other means. A lesion on the abdomen such as this may occur in three conditions, namely, mycosis fungoides—the diagnosis I favor in this case—lymphatic leukemia and sarcoma.

Leprosy (Mixed Type). Presented by DR. HOWARD FOX.

C. S., a man aged 39, was previously presented in January 1938 (ARCH. DERMAT. & SYPH. 38:100 [July] 1938). Since the last presentation the eruption has become more profuse and now shows an unusual geographic configuration. It is situated mainly on the anterior, lateral and posterior aspects of the trunk, to a lesser degree involving the buttocks and thighs. The eruption consists of annular lesions varying in diameter from 2 to 10 cm. The average width of the borders is about 1 cm. The borders are salmon colored, definitely infiltrated and slightly elevated above the surface of the skin. The central parts of the lesions are paler than the normal skin. In the center of some of the rings there are solid plaques of varying size and of the same color as the borders. Both the borders and the centers are anesthetic to the prick of a pin. Some of the lesions have coalesced and formed gyrate patterns. During the past two years the involvement of the hands has increased in severity. Two of the fingers were amputated for intractable swelling and ulceration.

Histologic examination of the border of a lesion on the trunk was made by Dr. D. L. Satenstein, who gave the following report: "Throughout the upper part of the cutis are many collections of the histiocytes in tubercle formation. About these is a moderate cellular infiltrate. In the remainder of the cutis there is some parenchymatous edema. Otherwise there is no change. The epidermis is comparatively thin, and in some areas the rete pegs and papillary bodies are missing. The tubercles are in part isolated and in part arranged in bandlike fashion. The histiocytes composing these masses have a granular or foamy cytoplasm, and the outlines are broken up. No organisms were found."

DISCUSSION

DR. FRANK C. COMBES: I was interested in the probability of a tuberculoid structure in these lesions. I was always under the impression that these cutaneous lesions of neural leprosy were of the vascular type and did not show any infiltration whatever, that is, that they were more or less identical with the lesions of a neurosyphilid.

A Case for Diagnosis (Acanthosis Nigricans?). Presented by DR. FRED WISE.

Miss F. I., aged 36, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 14, 1940, complaining of a dark brown discoloration on the face, which had first appeared three years ago. Her general health had always been good. She had always had a dark complexion and tanned readily. About three years ago, two teeth were extracted from the

left side of the upper jaw "because of a cyst" On the day after the extraction the left side of the face was swollen and inflamed Approximately two months later dark brown spots appeared on the skin adjacent to the nose and on both cheeks, chiefly affecting the skin around the mouth and the lateral aspects of the chin She was admitted to the New York Hospital for examination on May 30, 1938 There a complete physical check-up disclosed no significant deviations from normal health

Examination shows an area of dark brown pigmentation on both sides of the midportion of the nose, an inch (2.5 cm) above the alae nasi, and broad areas of hyperpigmentation around the mouth, extending from the nasolabial folds toward the lobes of the ears and involving the lateral aspects of the chin The surface of the affected areas is soft to the touch but has a definitely rugose appearance, resembling finished pigskin There also appears to be a faint periorbicular hyperpigmentation but without apparent alterations in the surface of the skin in these areas The borders of the peribuccal lesions are ill defined on the cheeks and chin, and the color fades out toward their peripheries

Histologic examination of a section of hyperpigmented skin showed "melanosis, probably preceded by an inflammatory process" (Dr D L Satenstein and Dr Wilbert Sachs)

DISCUSSION

DR EUGENE F TRAUB I suggest the possibility of acanthosis nigricans, because of the slight changes in the axillas I thought the skin was not merely pigmented but thrown into verrucous folds and thickened I do not think the condition is an ordinary pigmentary disturbance of the skin but one associated with some internal constitutional disease

DR A BENSON CANNON I have 2 patients under treatment for a pigmented condition exactly like that in this patient, a condition I have found to be due to the use of a commercial eau de cologne The location, distribution and character of the pigmentation all favor a cosmetic as being the most likely cause One of my patients had been thoroughly peeled on two occasions, first at a beauty parlor and later by a dermatologist, and in the first instance the condition was much aggravated I find that such pigmented areas in women are not uncommon I have had the most success by the use of remedies that cause a slight desquamation of the skin without producing too much local irritation The character of the pigmentation in this case in no way resembles that seen after the taking of phenolphthalein, and I should discount that drug as being a possible cause

DR GEORGE C ANDREWS I do not feel that this case is one of perfume dermatitis, because the color is too dark, being a slate color, which is the color of a phenolphthalein reaction I asked the patient if she took any laxatives, and she said she did occasionally I asked her what type of laxative she took, and she replied "ex-lax" and magnesia magma The other two suggestions of acanthosis nigricans and perfume dermatitis should, of course, be kept in mind

DR R H RULISON I was with Dr Andrews when the history of ingestion of phenolphthalein was obtained I favor the diagnosis of acanthosis nigricans because of the verrucous nature of the eruption

DR PAUL E BECHET It seems to me that there are definite points against the diagnosis of a phenolphthalein eruption These are the absolute symmetry in distribution, the tremendous pigmentation (almost black), the velvety papillomatous growth and the apparent lack of any cutaneous or subcutaneous inflammation While I have, of course, seen phenolphthalein eruptions which were dark, they were, however, of a dusky brownish red and never black I do not believe that the condition is due to a chemical reaction from cosmetics The evidence in favor of the diagnosis of acanthosis nigricans of the juvenile type is not convincing, but the suspicion remains If the same degree of pigmented, velvety, rugose papillomatosis occurred in the axillas or beneath the breasts, that diagnosis would immediately suggest itself After weighing the clinical evidence carefully, one cannot completely dismiss this suspicion

DR. HOWARD FOX: This eruption is not solely a hyperpigmentation. There is evidence of inflammation and unquestioned thickening of the skin. The condition is certainly not argyria or, in my opinion, an eruption due to phenolphthalein. The latter condition occurs in patches which are fairly well demarcated and which do not fade into the surrounding normal skin as do the lesions in this case. If the lesions had been present in the axillas, no one would have questioned the diagnosis of acanthosis nigricans. However, I have never seen this disease on the chin or cheeks and feel doubtful about the diagnosis.

DR. A. BENSON CANNON: Will Dr. Wise comment on the apparent good health of this woman for one who has acanthosis nigricans following a carcinoma?

DR. GEORGE C. ANDREWS: I have seen thickening of the skin due to rubbing in cases of phenolphthalein eruption. I admit that the thickening here does not look like lichenification. The condition has the velvety appearance of acanthosis nigricans, it is true, but the more common disease would be an eruption due to phenolphthalein, and she gives a history of having taken phenolphthalein.

DR. FRED WISE: I have never observed any phenolphthalein eruption resembling this condition, with respect to either color or conformation, and I should discard that tentative diagnosis. As to general health, I think most patients with early manifestations of acanthosis nigricans who have no visceral lesions are apparently in good health.

Extensive Acrodermatitis Chronica Atrophicans in a Man. Presented by

DR. PAUL E. BECHET.

H. E., a man aged 50, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 16, 1940, complaining of tightness of the skin of his feet and legs. The eruption began twenty-two years previously on the dorsal surfaces of the feet. During eighteen years the condition spread slowly but steadily, until the entire lower extremities from just above the lumbosacral region of the back to the toes present a symmetric involvement. There has been no change in the eruption in the past four years. The surface of the skin is glossy, atrophic and hairless. There are areas of telangiectasia, and the surface blood vessels are prominent beneath the thinned integument. Several areas are atrophic, and others suggest sclerodermatous changes, particularly about the ankles and dorsal surfaces of the feet. The Wassermann and Kahn reactions were negative. The urine was normal. The histologic report agreed with the clinical diagnosis.

DISCUSSION

DR. HOWARD FOX: Though this disease usually occurs in women, it also affects men occasionally, as in a patient of mine previously presented before this society (ARCH. DERMAT. & SYPH. 24:1129 [Dec.] 1931). The disease does not seem to shorten life or affect the general health. However, it may cause a good deal of annoyance or even disability from ulcerations, especially over the malleoli, where the skin is tightly stretched and easily traumatized. Such ulcerations are apt to last for many months and constitute the only serious feature of the disease.

Cheilitis. Presented by DR. EUGENE F. TRAUB.

H. Z., a youth aged 19, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on March 11, 1940, with an eruption about the lips of two and one-half years' duration.

Examination shows about the lip a well defined, erythematous, edematous, fissured, slightly crusted and scaly circumscribed patch. The right inner surface of the lower lip shows a raised oval lesion. There is an ill defined macular eruption about the tip of the nose extending downward to the sides and involving the nasolabial folds. The tongue is smooth, erythematous, enlarged and fissured. About the index and middle fingers, which are symmetrically involved, especially on the right hand, there is an ill defined erythematous thickened, lichenified and scaly patch on the inner surfaces. There are moderate scaliness and maceration between the fourth and fifth toes.

The patient smokes Philip Morris cigarets and uses Dr Lyons' tooth powder. He eats a well balanced diet. Patch tests were made with Philip Morris cigaret paper and gave negative results, but tests with Philip Morris tobacco gave positive results. Patch tests were also made with Pall Mall cigaret paper and tobacco, but the results have not yet been read. The Wassermann and Kahn reactions were negative.

Leprosy with Juxta-Articular Nodes Presented by DR FRED WISE

In October 1939 I presented a woman with leprosy associated with large juxta-articular nodes at the elbows (ARCH DERMAT & SYPH 41 789 [April] 1940). At that time several members said they did not think the nodules around the elbows were manifestations of leprosy. Strange to say, the injections of chaulmoogra oil partly cleared up the cutaneous lesions and caused considerable diminution in the size of the nodules.

Leukemia of the Skin Presented by DR EUGENE F TRAUB

E D was previously presented before the Atlantic Dermatologic Conference on March 9, 1940 (ARCH DERMAT & SYPH 42 687 [Oct] 1940) with typical leukaemia cutis with bullous lesions in some areas and solid masses in others. The condition was thought by some of the members to be leukemid rather than true leukaemia cutis. To confirm or refute this supposition, several biopsies were performed, with one specimen from an area on the vulva and another specimen from a lesion on the arm. The histologic diagnosis was leukaemia cutis.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

E WILLIAM ABRAWOWITZ, M D, *Chairman*

LEWIS B ROBINSON, M D, *Secretary*

May 7, 1940

A Case for Diagnosis (Mycosis Fungoides?) Presented by DR ABRAHAM WALZER

M S, a woman aged 32, is presented from Beth Moses Hospital. The past history is irrelevant. An eruption began four or five years ago with the development of three small spots, one on the right cheek, one on the left breast and one on the left forearm. Within three months the eruption had become widespread, covering the upper and lower extremities and the trunk in irregular patches of papulovesicular oozing dermatitis. She was treated in various local institutions with external and internal medication. The condition never completely cleared up, faintly brownish pigmented spots remained. For six months the patient was fairly well, with only a small spot here and there. Since then she has had numerous outbreaks, but none has been as serious as the first one.

The present eruption is of about one year's duration. The lesions are limited to the right cheek, the right arm and both breasts, particularly in the areolar areas. The trunk and extremities show many faintly pigmented patches of various sizes, the remains of previous lesions. The elementary lesion is a small pruritic papule or papulovesicle, varying in size from that of a pinhead to that of a lentil. These papules combine into patches forming oozing, elevated lesions from the size of a dime to that of a quarter. In some locations these lesions are arranged in semiannular formation (on the right arm). Some of them are covered with an impetiginous crust, while others have a papillomatous surface.

Complete physical examination showed no abnormalities aside from the cutaneous condition. The liver and spleen were not enlarged, but the axillary nodes were somewhat enlarged. The Wassermann reaction was negative. The

urine was normal, and the blood count on various occasions was also normal. Studies of the bone marrow showed no abnormality. Smears from the lesion on the breast showed no fungi.

Histologic examination of a specimen taken from the lesion on the breast showed acanthosis of the epidermis, especially of the rete pegs, and small and large vesicles in the upper layer of the epidermis. The basal cell layer was intact. Mitotic figures were scattered throughout. In the cutis there was dilatation of the vessels, with interstitial edema and an infiltration of pleomorphic cells, consisting of round cells, plasma cells, histiocytes, eosinophils and large reticular cells.

DISCUSSION

DR. J. FRANK FRAZER (by invitation): On the basis of the histologic picture, before I saw the patient, I had concluded that the condition might be mycosis fungoides. After seeing the patient I am willing to admit that the gross appearance of the lesions does not harmonize with that view. Nevertheless, I still favor the diagnosis of mycosis fungoides.

DR. FRED WISE: I suggest careful, repeated bacteriologic examinations.

DR. HERMAN GOODMAN: Did the patient present a generalized eruption which cleared up spontaneously?

DR. ABRAHAM WALZER: The disappearance was not spontaneous.

DR. HERMAN GOODMAN: What treatment was effective?

DR. ABRAHAM WALZER: Treatment consisted of many types of applications.

DR. HERMAN GOODMAN: Did the condition clear up under roentgenotherapy?

DR. ABRAHAM WALZER: The lesions did not respond to roentgenotherapy.

DR. GEORGE C. ANDREWS: I should like to ask Dr. Walzer how much roentgenotherapy this patient had. What were the dosage and the intervals?

DR. CHARLES WOLF: At present any diagnosis would be speculative. So far, none of the features of a lymphoblastoma have been revealed, and the only suggestive feature is the microscopic picture. However, the clinical aspects are diametrically opposite to what is to be expected in any of the lymphoblastoma group. The diagnosis of mycosis fungoides has been made tentatively. None of the features seen in that condition has been noted in a period of five years. The itching is slight, and there is no infiltration. Thirdly, the lesions are bullous. Furthermore, the response to roentgen rays is one of the specific phenomena in mycosis fungoides or leukemia. The leukemic picture here is also all on the negative side. Puncture of the marrow gave negative results, and the blood picture has been consistently normal. The lesions do not appear to be those of leukemia or of leukemid. Hodgkin's disease certainly does not produce phenomena as seen in this case. The clinical picture is of a circinate, papulovesicular eruption which clears intermittently and does not produce any systemic disturbances. I therefore suggest the diagnosis of chronic erythema multiforme or, possibly, dermatitis herpetiformis.

DR. DAVID L. SATENSTEIN (by invitation): The clinical features, the microscopic picture and the history do not fit in with any diagnosis mentioned. Dr. Eller's case of iododerma tuberosum is no doubt familiar. The history and the clinical and histologic pictures suggest iododerma.

DR. J. FRANK FRAZER (by invitation): Dr. Satenstein just stated that he saw nothing in the histologic picture that looked like mycosis fungoides. I should like to know how he interprets the nests of reticular cells with hyperchromatic nuclei and mitotic figures which dominate the picture.

I recall Dr. Eller's case. I opened the discussion on it when Dr. Eller read his report before the American Dermatological Society. I stated then that the histologic picture was "exactly the same as that seen in the tumor stage of mycosis fungoides" (ARCH. DERMAT. & SYPH. 24:777 [Aug.] 1931). This view was not challenged. Dr. Wile in discussing the case said he was "entirely in accord" with my view. He also stated that he did not think that the case was a true iododerma.

DR ABRAHAM WALZER This patient has been under observation for over four years. She refused to permit a biopsy for a long time and therefore continued to visit various institutions without receiving any definite diagnosis. Answering Dr Goodman's question about therapy, I meant that I used all the ordinary remedies employed in various clinics, such as ointments, pastes, dyes and lotions, giving them at various intervals. There was no apparent immediate result. The lesions would eventually clear up, and the last treatment she had had was credited with the cure, but the condition always recurred. Concerning the question of roentgenotherapy, I did not give her any. Before she returned to the Beth Moses Hospital seven months ago she had been treated by a roentgenologist in Brooklyn, who gave her four treatments at weekly intervals, without any apparent results. The question of pruritus has been raised. She has itching, as is evidenced by scratch marks, though it is not as intense as one would expect in mycosis fungoides. In my tentative diagnosis of lymphoblastoma, I excluded Hodgkin's disease, leukemia and lymphosarcoma. I suggested mycosis fungoides tentatively because a pathologist suggested the possibility of Hodgkin's disease. Mycosis fungoides, if it is a lymphoblastoma, is a primary lymphoblastoma of the skin. On the other hand, Hodgkin's disease is an internal disease, and the lesion of the skin is secondary. Therefore, if this condition were Hodgkin's disease, one would expect internal involvement. If it is mycosis fungoides, it is in the prefungoid stage, before infiltration has occurred, and one would not expect any of the internal manifestations of mycosis fungoides now, they occur at the terminal stage, if at all. As to the ingestion of iodides and bromides, I went into that question carefully. I suspected drugs, especially iodides. She states that she has not taken any drugs. She was warned not to take any. She recently refused to take capsules which her physician prescribed for a cold. Mycosis fungoides can exist in such a stage for twenty-five years, so that the question of time does not enter into the discussion. I still think that clinically the condition is certainly not mycosis fungoides, but the histologic picture suggests it. About the question of a bacterial investigation, numerous smears and cultures were made, but only some nonpathogenic organisms were obtained.

A Case for Diagnosis (Erythema Multiforme?) Presented by Dr JACOB SKLER (by invitation)

D C, a woman aged 43, is presented from Cumberland Hospital, for Dr David M. Davidson. The eruption began five years ago in the fall of the year and then cleared up. There was a recurrence the next year, and then the lesions again disappeared. For the past three years there have been recurrent crops of lesions, which have not cleared up completely. The eruption began on the ankles and spread upward to involve the legs, thighs, abdomen and breasts.

Examination shows numerous circinate and gyrate lesions with vesicular and bullous borders and flat erythematoviolaceous centers. The itching is severe and at times intolerable. The patient states that the eruption is aggravated or improved according to the weather, being more severe in damp and rainy periods. The eruption appears in crops, with remissions every two weeks.

The Wassermann reaction was negative. The urine was normal. Chemical examination of the blood showed 93 mg of sugar, 12.5 mg of urea nitrogen, 14 mg of creatinine and 3.4 mg of uric acid per hundred cubic centimeters. A blood count showed 82 per cent hemoglobin and 4,000,000 erythrocytes and 9,700 leukocytes per cubic millimeter, with a differential count of 67 per cent neutrophils, 3 per cent eosinophils, 25 per cent lymphocytes and 5 per cent mononuclear leukocytes. Examination for tinea gave negative results. A patch test with potassium iodide gave negative results. The histologic diagnosis was erythema multiforme.

DISCUSSION

DR EUGENE T. BERNSTEIN I consider this case to be one of erythema multiforme, not of the Hebra variety, due to ingestion of some drug. The patient claims that she took a bromide.

DR. DAVID M. DAVIDSON (by invitation): I was unable to obtain a history of ingestion of drugs. According to the record, the patient was treated once with strontium bromide. The condition did not become worse, nor did it improve much.

DR. E. WILLIAM ABRAMOWITZ: Regarding a history of drug ingestion, the patient volunteered that she had been taking all kinds of bromide preparations in the past but none recently. It is known that a bromide eruption can appear long after administration of the drug is discontinued. There is still a possibility that this condition may be a drug eruption. Has an analysis of the urine for bromides or iodides been made in this case? If not, I think that it should be and that the patient should receive intensive sodium chloride therapy.

DR. FRED WISE: For what was she taking bromides for some?

DR. E. WILLIAM ABRAMOWITZ: She said she was taking the bromides for some kind of nervous spells. I asked her about using iodized salt, and she said she had not used any. She is well informed on the subject, perhaps so much so that her eruption may be induced.

DR. JACOB SKEER (by invitation): If this woman appears well informed, she has received all her information from my associates and me. We also suspected a drug eruption and cautioned her against taking any drugs. We do not know whether she has taken any drugs, but as far as we can find out, she has not. The strontium bromide was given at the hospital for the itching and sleeplessness, and she seemed to feel better after it. Any drug she has had has been taken since the onset of the eruption.

Hypertrophic Scarring Following Eczema Vaccinatum. Presented by Dr. JACOB SKEER (by invitation).

M. B., a woman aged 40, is presented from Cumberland Hospital, for Dr. David M. Davidson. The patient states that an eczematous eruption developed on her neck about the middle of January 1940, presumably caused by a new sweater. The eruption then spread to the upper part of the chest and the arms. Three weeks later her two children were vaccinated. About eight to ten days later, blisters appeared on the patient's neck, and she applied to the Emergency Room of the Cumberland Hospital for treatment on February 16. The skin of the neck and arms was an angry red, and numerous vesicles were present. Her temperature was 100 F. She was sent to Kings County Hospital and was transferred to the Kingston Avenue Hospital. On admission she presented, according to the records, a vacciniform eruption consisting of numerous scattered, discrete and confluent, umbilicated pustules surrounded by an erythematous areola, situated on the neck, the upper part of the chest and the arms. The temperature was 105 to 106 F. There was a submaxillary and cervical adenitis. The blood count showed 4,300,000 erythrocytes and 12,000 leukocytes per cubic millimeter. The urine was normal. The temperature remained at 105 to 106 F. for nine days, after which it fell to 100 F. and then became normal in four days. The patient remained in the hospital for six weeks and was then discharged. She states that she was vaccinated during childhood but it "did not take." There was no vaccination scar present.

Examination at the present time shows widespread hypertrophic erythematous scarring, involving the neck like a collar and the upper part of the chest. On the arms and chest are numerous hypertrophic and atrophic scars, the sites of the vacciniform lesions. Movement of the neck is inhibited and limited, owing to the scarring.

DISCUSSION

DR. ABRAHAM WALZER: I treated this patient for almost seven weeks at the Kingston Avenue Hospital. She had a high temperature, and there was a suspicion at one time of smallpox. The question of eczema vaccinatum is interesting, because there seems to have been an increase in its incidence in the past few years. At least, I have encountered 5 or 6 cases in the last year or two. It was first described in 1887 by Kaposi, who thought it was due to a fungous infection. A few years

later Juliusberg described it under the name pustular vacciform eruption. At present this condition is included under postvaccinal eruptions. There are a number of types of such eruptions. One represents the hematogenous spread of the virus from the site of vaccination, causing true generalized vaccinia. Occasionally attacks of urticaria or erythematous eruptions which are also due to dissemination of the virus are encountered. Another type is due to the spread of the virus from one site to another, or contact infection, such as occurs when a child touches the site of vaccination and then touches another part of the skin, close by or far away. Here a group of these vacciform eruptions develops. The third type is that in which there is an introduction of the virus into the system through a diseased site, as in this instance. That is serious. The mortality is about 50 per cent. That is one reason why infants with eczema should not be vaccinated or allowed to be near people who have been vaccinated. When the virus gets into such an eczematous lesion, it is said that there is a tremendous increase in local production of the virus, and the system is overwhelmed under this high dose, with a resulting terrific reaction, such as this woman had. There is the fourth type, in which there is secondary infection on top of a vaccination, such as impetigo. Tuberculosis and even syphilis have been described. There is still another type, which probably should not be included here but which is described with postvaccinal eruptions. Occasionally lichen planus will develop in a child after a vaccination, or pemphigus or psoriasis, but those, of course, have nothing to do with this case. At the Brooklyn Jewish Hospital about ten days ago I saw a 6 month old baby with this condition who died.

DR SEYMOUR H. SILVERS: I saw this patient at the Kings County Hospital before she was sent to the Kingston Avenue Hospital. In fact, I was responsible for her transfer. The lesions I saw were those usually seen in vaccinia. In vaccinated children, first a papule is observed, and then a vesicle, followed by a pustule, ulceration and crusting. This patient showed lesions in these various stages over the body, but on the neck there was a gangrenous mass. I believe that while she was at the Kingston Avenue Hospital she received either sulfanilamide or sulfapyridine. She has lost a great deal of weight since I first saw her.

DR ADOLPH ROSTENBERG: I have no doubt that this case is one of eczema vaccinatum due to accidental contact with the children who had been vaccinated. I remember a boy with an eruption similar to this and with constitutional symptoms, and he died. The keloidal formation reminds me of a patient presented a few weeks ago with keloid formation following herpes zoster. I think in these deep destructions keloids develop, perhaps, in persons who have a tendency toward keloid formation.

DR E. WILLIAM ABRAMOWITZ: Has Dr. Rostenberg any suggestions for treatment?

DR ADOLPH ROSTENBERG: The only suggestion I have for treatment is roentgenotherapy, it should have been started early.

DR EUGENE T. BERSTEIN: I should like to suggest a possible explanation for the development of these hypertrophic or keloidal scars. The patient had severe itching and scratched herself a great deal, and through this trauma these keloidal scars developed.

DR DAVID M. DAVIDSON (by invitation): I should like to hear more suggestions for therapy. The most important thing to me now is what to do with this patient. Is the problem one for roentgenotherapy or for plastic surgery?

DR ABRAHAM WALZER: In answer to Dr. Silvers, this woman received sulfapyridine for five days but became cyanotic and showed other toxic symptoms, and its administration had to be stopped. As for the hypertrophic scars or keloids, I do not believe one can incriminate any treatment or any type of trauma. I believe it is an inherent tendency. In a certain percentage of people keloids or hypertrophic scars develop no matter what the type of treatment or type of injury has been. This woman has this tendency to keloid formation.

DR. HERMAN GOODMAN: This woman has no keloids. She had injuries down to the true skin. There are eight or nine depressed areas on the chin. The edge of the normal skin is higher than the places where the skin was injured by the vaccinia. If she had a tendency to keloid formation, every injury to the true skin should show a raised lesion. She had a gangrenous-like eruption which led to the exposure of the deeper tissues. The resulting scars contracted and pulled the face and chin down to the neck. She has a contracting scar of the neck. No hypertrophic scars are visible in places where the true skin was injured.

Senile Elastosis. Acrodermatitis Chronica Atrophicans. Presented by **DR. ABRAHAM WALZER.**

M. C., a man aged 63, is presented from Brooklyn Jewish Hospital, complaining of an eruption of many years' duration, involving the face, neck, ears, trunk and lower extremities. The patient is a carpenter. He first came to the clinic a year ago, complaining of an infection on his right cheek, of pigmented patches on the face and neck and of lesions on the lower extremities. Examination shows the scar on the right cheek resulting from the infection. The pigmented patches he complains of are seen on the back and sides of the neck, in the eyebrow area, on the skin adjacent to the inner canthus of each eye and on the helix and anthelix of each ear. The color varies from ivory white on the ears and in the eyebrow area to yellow on the neck. The white areas are smooth, soft, sharply outlined and not elevated or only faintly elevated. The patch on the neck feels thickened but soft, and the natural cutaneous folds are accentuated. There is no suggestion of a papule as the elementary lesion, although there are a few scattered pigmented points (level with the skin) surrounding the patch on the neck. The skin of the face is thinned, with the vessels shining through. On the posterior part of the hard palate and on the soft palate is a patch composed of telangiectatic points on a yellow pigmented surface. The sides of the tongue are also tinged light yellow.

On the lower half of the trunk and on both lower extremities, extending to the toes, is an extensive diffuse atrophic dermatitis. All stages of this dermatitis can be seen, from bright red to dusky blue erythema and from raised, inflammatory boggy patches (lumbar region) to thin, wrinkled skin. The subcutaneous veins stand out prominently.

The icteric index and the values for total and free cholesterol and for sugar were within normal limits. A section taken from the lesion on the neck showed atrophy of the epidermis, with flattening and disappearance of the papillae. Immediately beneath this was a mass of degenerated elastic tissue extending across the section in a bandlike area. The elastic fibers were thickened, broken and twisted. The blood vessels and appendages showed no changes.

Pseudo Xanthoma Elasticum with Angioid Streaks of the Retina. Presented by **DR. SEYMOUR H. SILVERS.**

A. D., an unmarried man aged 43, residing in the United States for the past seventeen years, is presented from Beth Israel Hospital, complaining of generalized itching of two years' duration and of imperfect vision. Examination shows a well developed man who presents on both sides of the neck, extending to the face and down to the clavicles, ill defined patches devoid of hair and having a velvety texture. The color varies, ranging from light yellow to lilac. The follicular openings are prominent. Definite papules cannot be felt. The left axilla shows a similar velvety patch about the size of a palm, which is also devoid of hair but is grayish white. A similar patch is present in the right axilla. Examination of the retina shows numerous hemorrhagic streaks. Varying retinal lesions resulting from former hemorrhages have been seen at previous examinations. The patient's vision is gradually diminishing, and he is unable to follow his trade as a cook.

A blood count was normal except for eosinophilia (9 per cent eosinophils). The urine was normal. The Wassermann and Kahn reactions were negative. The amounts of dextrose, urea, nonprotein nitrogen, calcium and cholesterol in the blood were within normal limits. There were no parasites in the stool. Roentgen examination of the bones failed to show Paget's disease. The arteries of the legs showed calcification. Histologic examination of a section of skin showed typical pseudo xanthoma elasticum.

DISCUSSION OF PAPERS BY DR WALZER AND DR SILVERS

DR SEYMOUR H SILVERS In this condition, the cutaneous lesions are only one part of the syndrome, which is known as the syndrome of Groenblad and Strandberg. The cutaneous lesions are the less important part of the syndrome. The more important part is the condition in the eye. The diagnosis of this syndrome was made by the ophthalmologist at the hospital on examination of the fundi, before the skin was examined.

DR HERMAN E WOLFE (by invitation) I should like to say a word about the pathologic changes underlying the lesions of the retina. Between the retina and the choroid is a thin glassy membrane containing elastic tissue which is known as the lamina vitrea. In this membrane in this case the elastic tissue is destroyed, and cracks and fissures are produced. On looking into the eye with the ophthalmoscope these cracks or fissures are seen as gray to black to brown lacework, resembling vessels, which are neither in the choroid nor in the retina but somewhere between. These are the so-called angioid streaks. I have photographs here showing these streaks. There is a lacy network adjacent to the optic nerve which extends to the periphery. The retinal vessels are not involved in this particular condition. Lewis and Clayton (*ARCH DERMAT & SYPH* 28 546 [Oct] 1933), however, reported that there was destruction of the elastic components of the vessels. That is probably so, since it is the only way to explain the hemorrhages which occur in the eyegrounds. The macula, which has to do with central vision, is usually involved. In this case, a mound projecting into the vitreous can be seen. This is due to hemorrhage, organized tissue and elastic tissue debris. The vision, of course, in this particular eye is completely lost and has been so for the past twenty-five years. In the other eye, subsequent examinations have disclosed small flame-shaped hemorrhages between the temporal arches. This indicates that the condition will follow the same relentless course as in the other eye.

An interesting feature is that frequently this condition is seen without pseudo xanthoma elasticum but rather with Paget's disease, which is an osteoporosis. What interested me in looking over the literature was this. In spite of the fact that pseudo xanthoma elasticum is comparatively rare, Dr Goedblad of Leyden, in tracing back 67 cases, found angioid streaks associated with the pseudo xanthoma elasticum in 57 cases. This disparity interested me.

DR E WILLIAM ABRAMOWITZ How many eyes examined post mortem have showed angioid streaks in the retina?

DR HERMAN E WOLFE (by invitation) About twenty-five eyes examined post mortem have showed this condition.

DR JACOB SKLER (by invitation) Just as angioid streaks of the retina may occur without pseudo xanthoma elasticum, it is known also that pseudo xanthoma elasticum may occur without angioid streaks. A report made recently stated that angioid streaks of the retina accompanied pseudo xanthoma elasticum in only about 25 per cent of the cases (Sweetzer, S E, and Laymon, C W. *Pseudoxanthoma Elasticum*, *Brit J Dermat* 45 512, 1933).

DR ABRAHAM WALZER Two conditions which are often confused histologically are pseudo xanthoma elasticum and senile elastosis. They are often difficult to differentiate. In pseudo xanthoma elasticum the fibrous bands are often in nodular formation and deep in the cutis, whereas in senile elastosis the picture is almost identical, but higher up, in the upper layers of the cutis. The clinical picture in senile elastosis is almost like that of pseudo xanthoma except that in the latter the elementary lesions are papules, because the lesion is a true elastoma—a true

elastic tissue tumor—whereas in senile elastosis there is no elementary papular lesion, since the increased amount of elastic tissue is not due to a production of new elastic tissue but only to a destruction of the connective tissue, which induces the elastic tissue to appear prominent. The lesion is, therefore, not an elastoma at all. As to the location of the lesions, in pseudo xanthoma elasticum the lesions are usually on the covered parts of the body, as for instance in the axillas and on the inner aspect of the arm, whereas in senile elastosis they are usually on the parts exposed to the elements. Pseudo xanthoma occurs early in life, while senile elastosis occurs usually after the age of 40. It is extremely rare to encounter 2 cases like these presented at a meeting together.

Xanthoma Diabeticorum. Presented by DR. SEYMOUR H. SILVERS.

D. S., a girl aged 15, is presented from King's County Hospital. She has been known to have diabetes for three years and has received approximately 30 to 40 units of protamine zinc insulin daily, with no restriction as to diet. About five months ago the patient noticed small white or pale pink pimples on her elbows. These gradually progressed in size, some coalescing to form small tumor masses, as they did on her lower extremities and buttocks, and persisting up to the present. She complains of polyuria and polydipsia. The past history is not significant except for the diabetes. Her family history is irrelevant.

Physical examination gave essentially negative results except for the cutaneous lesions. She is well developed and well nourished. There is hyperemia of the face. Situated around the elbows and other points of the body, as well as on the buttocks, are numerous bilateral and symmetric reddish yellow, pea-sized, discrete nodules.

Urinalysis showed a 4 plus reaction for sugar and a 1 to 4 plus reaction for acetone but no albumin. The Wassermann reaction of the blood was negative. Chemical examination of the blood showed 228 mg. of sugar, 22 mg. of uric acid, 1.17 mg. of creatinine and 296 mg. of cholesterol per hundred cubic centimeters. The plasma carbon dioxide amounted to 50 per cent. A blood count showed 75 per cent hemoglobin and 3,500,000 erythrocytes and 8,200 leukocytes per cubic millimeter, with a differential count of 45 per cent polymorphonuclear leukocytes, 52 per cent lymphocytes, 2 per cent monocytes and 1 per cent transitional forms. The basal metabolic rate was $+7$ per cent. The icteric index was 4.5. A direct van den Bergh test gave a negative result. A test for bilirubin showed 0.2 mg. per hundred cubic centimeters of urine. Roentgenographic studies showed a small, shallow sella turcica, and internal hyperostosis of the frontal and parietal bones. The sinuses were small. There were no pulmonary or pleural changes. No abnormal mass or collection of fluid was seen in the abdomen. The observations were in line with cranial dysplasia, a form of hypopituitary disturbance.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: In view of the history of diabetes, with polyuria and polydipsia, and the bony changes, did Dr. Silvers consider the diagnosis of the Hans-Schiller-Christian syndrome?

DR. LOUIS TULIPAN: It appears to me that this condition is perhaps associated with some pituitary disturbance. I agree with what has been said. Some years ago I presented before this society a case of acromegaly with exactly the same picture (Tulipan, L.: Xanthoma Tuberosum Multiplex and Acromegaly, ARCH. DERMAT. & SYPH. 22:724 [Oct.] 1930). Chemical examination of the patient's blood showed 500 mg. cholesterol and 364 mg. sugar per hundred cubic centimeters. A year after I saw him he returned to Bellevue Hospital, and there was not a sign of any lesion on the body, whereas before he had been covered with lesions. He had had absolutely no treatment during that year. The lesions disappeared spontaneously.

DR. SEYMOUR H. SILVERS: I think it has been accepted that diabetes may be either of pancreatic or of pituitary origin. In young patients one is likely to find pituitary changes on the roentgenogram of the skull. Diabetes in a young girl like this would more probably be of the pituitary type.

Alopecia Cicatrisata (Pseudopelade of Brocq) Presented by DR ABRAHAM WALZER

A S, a married woman aged 42, is presented from Brooklyn Jewish Hospital with an eruption of the scalp of one and one-half years' duration. About twenty years ago the patient had an operation on the left mastoid, and two and one-half years ago she had an amputation of the cervix. The present trouble involves the scalp and extends from the temporal area to the region behind the mastoid on both sides. The patient says that these areas were never red or inflamed. The first thing she noticed was that the hair fell out slowly. At present these patches are white, glossy and faintly atrophic. No hair follicles are visible, and there are no "exclamation hairs" in the patches or in the borders. Hairs are scattered here and there in the bald areas.

Examinations of the hair for fungi and cultures of the hair showed no abnormalities. These observations were made on a section taken from the atrophic patch. There was a pronounced thinning of the epidermis with loss of papillae and complete absence of appendages. The collagen bundles were homogeneous, almost basophilic in staining affinity, and had completely lost their fibrillar character. Elastic tissue stain showed loss of the network in the subpapillary layers, but the elastic tissue in the deeper layers of the cutis appeared normal.

Alopecia Cicatrisata (Pseudopelade of Brocq) Presented by DR ABRAHAM WALZER

T F, a woman aged 39, is presented from the Brooklyn Jewish Hospital with an eruption of the scalp of two years' duration. The past history revealed nothing of importance. The alopecia began on the vertex and gradually spread forward and to the sides. There was no soreness or pruritus associated with the loss of hair.

Examination shows numerous patches of alopecia varying in size from that of a pea to that of a dime or a little larger and arranged in linear or irregular formations, with areas of normal skin and hair between. The borders of the patches are irregular with distinct jutting out here and there. The surface of the bald spots is ivory-like in appearance, with complete absence of follicular openings. No broken hairs are seen. On palpation a faint depression can be noted.

Examination of the hair for fungi and cultures gave negative results.

DISCUSSION ON CASES OF ALOPECIA CICATRISATA

DR MAX SCHEER. The latter case was a typical one of alopecia cicatrisata, presenting pronounced atrophy without inflammatory evidence. The former, in my opinion, is not one of alopecia cicatrisata. There is no atrophy at all. The condition is just an alopecia (probably, I think, alopecia areata).

DR ADOLPH ROSTENBERG. I agree with Dr Scheer. The characteristic feature in alopecia cicatrisata is the keratotic plug, which 1 of these patients showed but which was entirely absent in the other. In the second case the atrophy was pronounced, while in the first case the skin was smooth and showed no atrophy.

DR E WILLIAM ABRAWOWITZ. I should like to ask about the patient with patches on the sides of the scalp. This condition is frequently called alopecia ophiasique. Why does Dr Walzer call it alopecia cicatrisata?

DR MAX SCHEER. I have had occasion to follow some of these cases of alopecia cicatrisata, and the earliest lesion is as typical as the one in the second case. Even a lesion that is no bigger than $\frac{1}{8}$ or $\frac{1}{4}$ inch (0.3 to 0.6 cm) in diameter already has a white milky appearance. One never sees a lesion enlarge to $1\frac{1}{2}$ inches (4 cm) in diameter in the early stage with a normal-appearing skin.

DR ABRAHAM WALZER. One patient presents a typical example of this disease, but in the other the condition was only suggestive. For that reason, a section was removed for histologic study. I thought I saw faint depressions, and, in contradistinction to some of the discussion, there were definite areas with absence

of follicles. Of course, there were some hairs growing in the patch, and there were a few follicles noticeable. The histologic section showed distinct atrophy. Therefore, one must exclude alopecia areata, which never produces atrophy. So, because of the histologic picture and the peculiar clinical picture—the condition not being true alopecia areata—I feel that I am entitled to label the case one of pseudopelade of Brocq.

Lupus Vulgaris Disseminatus. Roentgen Ray Dermatitis? Pulmonary Tuberculosis. Presented by DR. GIRSCH D. ASTRACHAN (by invitation). L. Q., a man aged 57, born in Austria, was admitted to Metropolitan Hospital on March 26, 1940. He was previously presented by Dr. George M. Lewis before the Manhattan Dermatologic Society on April 11, 1939 (ARCH. DERMAT. & SYPH. 40:1065 [Dec.] 1939).

Since the previous presentation the blood count was found to be essentially normal. Chemical examination of the blood showed normal values for nonprotein nitrogen, sugar and creatinine, but the chlorides (as sodium chloride) amounted to 632 mg. per hundred cubic centimeters. The Wassermann and Kahn reactions of the blood were on one occasion weakly positive and doubtful, respectively, while one week later they were negative. The sputum showed tubercle bacilli. The tuberculin test in a dilution of 1 to 100,000 gave positive results. A roentgenogram of the chest (taken by Dr. Weinberg) showed probable caseous pneumonic tuberculosis, with cavitation in the right apex. Histologic examination (by Dr. Saccone) showed lupus vulgaris. The section showed small tubercles with giant cells of Langhans' type but no caseation.

DISCUSSION

DR. GIRSCH D. ASTRACHAN (by invitation): There are some interesting features in this case which I should like to mention. This patient had a weakly positive reaction to the Wassermann and Kahn tests of the blood on one occasion and a negative reaction the following week. This phenomenon may fit in with the well established fact that weakly positive nonspecific reactions occur in cases of tuberculosis. There is also a question as to the proper diagnosis of the ulcer on the right cheek. There is a possibility that the lesion is roentgen ray dermatitis, regardless of the fact that the most important symptom, namely, telangiectasia, is missing. Lupus vulgaris disseminatus usually appears in children following some xanthematic eruption. This factor is absent in this case. I feel, however, that because of the rapid development of the eruption on the back, this eruption can be called lupus vulgaris disseminatus. The case is presented mainly for therapeutic suggestions.

DR. CHARLES WOLF: It seems to me that the therapeutic approach in this particular case should offer no difficulty. Here is a man with active tuberculosis. His system is being fed constantly or periodically with streams of tubercle bacilli which are being disseminated. The thing to do here is to have the primary focus attended to, whether by pneumothorax, by removal of the patient to a high altitude or by generalized ultraviolet irradiation. I believe that systemic supportive treatment would prevent dissemination of tubercle bacilli from the pulmonary focus.

DR. HERMAN GOODMAN: Phthisiotherapists disapprove of giving a patient with active pulmonary tuberculosis any form of generalized irradiation. A nurse in a dermatologic clinic was given generalized ultraviolet irradiation without any previous examination. Acute pulmonary tuberculosis developed after one exposure.

DR. GEORGE M. LEWIS: While this patient was in the Neurological Hospital at Welfare Island, it was not certain that the ulceration on the right cheek was due to roentgen rays. However, the severe pain, for which he requested and received a large amount of sedatives, would indicate that this lesion was the roentgen rays even without the presence of telangiectasia. I believe it was the consensus at the time of the previous presentation that this lesion was a roentgen ray ulcer superimposed on lupus vulgaris. The roentgenotherapy was given in Vienna, Austria. He has consulted a great many physicians both here and abroad.

and has had many forms of treatment, including gold therapy, salt-free diet and injections of a bismuth compound. No benefit from the therapeutic endeavors was noted, rest in bed had absolutely no effect. I think his condition is worse now than when I last saw him, eight or nine months ago. Sanatorium treatment is probably indicated, or perhaps, as Dr Wolf suggested, a high altitude.

DR E WILLIAM ABRAMOWITZ. I should think that the prognosis in this case is poor now that there is beginning dissemination of the lesions. I had a patient with extensive lupus vulgaris of the face and neck following tuberculous mastoiditis (*ARCH DERMAT & SYPH* 15 351 [March] 1927). The lupus vulgaris healed completely under gold therapy. If this man has not had adequate gold therapy, I think it might be tried. There is nothing to lose.

DR GIRSCH D ASTRACHIAN (by invitation). This patient did not respond well to applications of Aloe vera leaves. He claimed, however, that while he was on the salt-free diet his condition seemed to improve somewhat. I think that the advice of Dr Wolf should be followed, that he should be given systemic treatment for the tuberculosis.

Erythema Figuratum (Erythema Annulare Centrifugum of Darier?) Presented by DR ABRAHAM WALZER

S M, a woman aged 37, is presented from the Brooklyn Jewish Hospital, for Dr David M Davidson, complaining of an eruption of four months' duration on the neck, the trunk and the extremities. The past history revealed nothing of importance. The eruption began near the right elbow as a red pruritic spot. Four days later it spread, and many other lesions appeared and extended all over the aforementioned areas.

On March 20, 1940, nine weeks after the appearance of the eruption, the patient first presented herself at the clinic. She showed an eruption consisting of pruritic pinhead-sized to pea-sized erythematous papules with fine scaling to silver dollar-sized annular or elliptic lesions with raised erythematous borders and clearing centers, some with light brown pigmentation. At present many of the lesions have disappeared, leaving fine wrinkling or pigmentation. The most outstanding lesions remaining are on the side of the trunk and hips, where by coalescence they form many marginate and gyrate lesions with raised erythematous borders and light brown centers.

Repeated scrapings of the lesions and cultures have failed to show fungi. Histologic examination showed an acute exudative process compatible with that seen in the erythema multiforme group of diseases.

Darier's Disease (Keratosis Follicularis) Presented by DR SEYMOUR H SILVERS

Miss W, aged 19, is presented from Kings County Hospital. Two years ago she noticed the gradual appearance of small pink pimples over the neck and shoulders. These increased in size and number. Many coalesced and changed in color. Later similar areas appeared on the forehead and temples. The lesions over the shoulders frequently became oily and scaly. The lesions are pruritic. The past history is irrelevant, and the patient is otherwise in good health. The patient's mother has had a similar condition of her skin for many years.

Examination shows over the face, neck and upper portion of the shoulders numerous papular pigmented lesions, through each of which a hair is seen to protrude. In some areas the lesions have coalesced to form small tumor-like masses.

The urine was normal. The Wassermann reaction of the blood was negative. The blood count was within normal limits, and chemical examination of the blood also showed normal results. Histologic examination showed keratosis follicularis.

Book Reviews

La maladie de Besnier-Boeck-Schaumann. By L. M. Pautrier, professeur de clinique des maladies cutanées et syphilitiques à la Faculté de Médecine de Strasbourg. Price \$2.05, paper. Pp. 344, with 105 illustrations. Paris: Masson & Cie, 1940.

In the preface Pautrier emphasizes the value of considering dermatology from the viewpoint of histophysiology, physiology, biology and general pathology.

Most illustrative of the value of the broader concept is Besnier-Boeck-Schaumann disease, a new reticuloendotheliosis. This disease can successively, simultaneously or separately invade all parts of the organism extending far beyond the limits of dermatology and including all branches of medicine.

The subject matter is divided into three parts. In the first part of Besnier-Boeck-Schaumann disease is discussed, including discussion of lupus pernio of Besnier and Tenneson, the sarcoids or miliary lupoids of Boeck and the benign lymphogranulomatosis of Schaumann. At first the disease was described as simple or separately by Boeck, and this description was later amplified by Boeck. It was Jorgen Schaumann who synthesized these lesions with multiple lesions of the lymphatic system and termed the disease "benign lymphogranuloma." Later he considered the disease to have a special predilection for the hemopoietic system and the cause to be tuberculosis of bovine origin.

The second part, on clinical manifestations, includes a detailed description of the disease as it affects the various tissues and organs and the principal syndromes produced thereby, in order. Lesions of the following structures are discussed: cutaneous teguments (nasal, rhinopharyngeal, palatine and buccal membranes); bone; muscles; lymphatic and hemopoietic organs (ganglions, tonsils, spleen and blood); respiratory system (lungs and tracheobronchial ganglions); viscera (heart, liver, kidneys, intestines and pancreas), and nervous system (eyes). In addition, infantile forms of the disease as recently reported are described.

In the third part miscellaneous subjects are discussed, such as pathologic-anatomic synthesis; reactions to tuberculin tests; general phenomena; variable modes of evolution and prognosis; age, sex and geographic distribution; etiology, treatment.

The essential characteristics of Besnier-Boeck-Schaumann disease are: the semiuniversal involvement of the organism, the multiplicity of the clinical manifestations resulting therefrom, its unusually benign and asymptomatic course and its variable evolution. The disease has frequently been mistaken for tuberculosis, especially when it involves the lungs or viscera and is unaccompanied by cutaneous or peripheral ganglionic manifestations. Rarely is it associated with tuberculosis. The pathologic picture of the disease is constant but not specific—it is at times exactly simulated by tuberculoid leprosy—and reveals it to be a disease of the reticuloendothelial system. Anergy to tuberculin, occurring in two thirds of the persons affected with the disease, is of some value in differentiating tuberculosis but does not indicate that the disease is of tuberculous nature. The cause of the disease remains unknown; virus infection is suggested. Females are more often affected. Treatment is difficult to evaluate, as unexpected spontaneous

resolution may occur. Local cutaneous lesions respond at times to repeated applications of solid carbon dioxide.

This monograph represents the culmination of constant research and study by the author in the subject for the past four years. It is accompanied by an extensive bibliography and is profusely illustrated by excellent clinical photographs, photomicrographs and roentgenograms. The volume is well edited, is free of typographic errors and is printed on paper of the best quality in clear and legible type.

CORRECTION

In the article by Dr. Herbert L. Traenkle entitled "Epithelioma Adenoides Cysticum, Trichoepithelioma and Basal Cell Cancer: Relation Between These Diseases, as Shown by Histologic Studies of Multiple Benign Cystic Epithelioma," in the November issue (*ARCH DERMAT & SYPH* 42:822, 1940), the first three illustrations have been incorrectly numbered. Figure 2 should be figure 1, figure 3 should be figure 2, and figure 1 should be figure 3. The legends as numbered in the *ARCHIVES* are correct.

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